=> fil reg; d stat que 17; d que nos 115; fil capl; s 115; fil uspatf; s 115 FILE 'REGISTRY' ENTERED AT 14:39:04 ON 30 APR 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 29 APR 2002 HIGHEST RN 409058-68-0 DICTIONARY FILE UPDATES: 29 APR 2002 HIGHEST RN 409058-68-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

VAR G1=14/20/25/30/35 VAR G2=H/X/19/CY NODE ATTRIBUTES: CONNECT IS E1 RC AT 19 DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 50

@30

STEREO ATTRIBUTES: NONE

L7 771 SEA FILE=REGISTRY SSS FUL L4

100.0% PROCESSED 1659 ITERATIONS

SEARCH TIME: 00.00.03

771 ANSWERS

Jones 09/716332 Page 2

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L4
                STR
L7
           771 SEA FILE=REGISTRY SSS FUL L4
L9
           1916 SEA FILE=REGISTRY ABB=ON C18H18N2O3/MF OR C18H18N2O3.BRH/MF
L10
           1973 SEA FILE=REGISTRY ABB=ON C18H18N2O3.CLH/MF OR C18H18N2O3.K/MF
                OR C18H18N2O3.NA/MF OR L9
T.11
             14 SEA FILE=REGISTRY ABB=ON L7 AND L10
L12
           3074 SEA FILE=REGISTRY ABB=ON 1H PYRROLE 3 PROPANOIC ACID
L13
              9 SEA FILE=REGISTRY ABB=ON L11 AND L12
L14
          70130 SEA FILE=REGISTRY ABB=ON 2 4 DIMETHYL
T.15
              3 SEA FILE=REGISTRY ABB=ON L13 AND L14
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FILE 'CAPLUS' ENTERED AT 14:39:05 ON 30 APR 2002
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FILE COVERS 1907 - 30 Apr 2002 VOL 136 ISS 18 FILE LAST UPDATED: 29 Apr 2002 (20020429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L16 10 L15

FILE 'USPATFULL' ENTERED AT 14:39:05 ON 30 APR 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 25 Apr 2002 (20020425/PD)
FILE LAST UPDATED: 25 Apr 2002 (20020425/ED)
HIGHEST GRANTED PATENT NUMBER: US6378132
HIGHEST APPLICATION PUBLICATION NUMBER: US2002049999
CA INDEXING IS CURRENT THROUGH 25 Apr 2002 (20020425/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 25 Apr 2002 (20020425/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2002

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>>> USPAT2 is now available. USPATFULL contains full text of the <<< >>> original, i.e., the earliest published granted patents or <<< >>> applications. USPAT2 contains full text of the latest US <
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publications, starting in 2001, for the inventions covered in
                                                                        <<<
    USPATFULL. A USPATFULL record contains not only the original
>>>
                                                                        <<<
     published document but also a list of any subsequent
>>>
                                                                        <<<
    publications. The publication number, patent kind code, and
>>>
                                                                        <<<
>>>
     publication date for all the US publications for an invention
                                                                        <<<
>>>
     are displayed in the PI (Patent Information) field of USPATFULL
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    records and may be searched in standard search fields, e.g., /PN,
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    /PK, etc.
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>>>
    USPATFULL and USPAT2 can be accessed and searched together
                                                                        <<<
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     through the new cluster USPATALL. Type FILE USPATALL to
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     enter this cluster.
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    Use USPATALL when searching terms such as patent assignees,
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    classifications, or claims, that may potentially change from
                                                                        <<<
    the earliest to the latest publication.
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This file contains CAS Registry Numbers for easy and accurate substance identification.

L17 6 L15

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=> dup rem 116,117
FILE 'CAPLUS' ENTERED AT 14:39:14 ON 30 APR 2002
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```

FILE 'USPATFULL' ENTERED AT 14:39:14 ON 30 APR 2002 CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS) PROCESSING COMPLETED FOR L16 PROCESSING COMPLETED FOR L17 T.18 16 DUP REM L16 L17 (0 DUPLICATES REMOVED) ANSWERS '1-10' FROM FILE CAPLUS

ANSWERS '11-16' FROM FILE USPATFULL

=> d ibib abs hitstr 118 1-16; fil cao; s 115

```
L18 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                        2002:184907 CAPLUS
                        136:241643
```

DOCUMENT NUMBER:

Exemestane as chemopreventing agent TITLE:

INVENTOR(S): Di Salle, Enrico; Piscitelli, Gabriella; Massimini, Giorgio; Purandare, Dinesh; Martini, Alessandro;

Muggetti, Lorena

PATENT ASSIGNEE(S): Pharmacia + Upjohn S.p.A., Italy; Pharmacia + Upjohn

Company

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.					KIND DATE				A									
WO 2002020020					1	2002	0314		WO 2001-EP10172 20010831									
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
						DE,												
		GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	
						MA,												
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	

```
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
    DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
    BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
```

PRIORITY APPLN. INFO.: US 2000-658052 A 20000908

The present invention concerns the use of aromatase inhibitor exemestane, either alone or in combination with other therapeutic agents, in the chemoprevention of estrogen dependent cancer in mammals, including humans, at increased risk of the disease. Exemestane treatment (4, 20 or 100 mg/kg/wk, IM), started 1 wk after dimethylbenzanthracene (DMBA) exposure (20 mg/rat, PO) and continued for 19 wk, significantly decreased tumor incidence from 85 % in vehicle treated rats to 13.6 % in the 100 mg/kg treated group. Moreover, exemestane at 100 mg/kg reduced significantly the tumor multiplicity, being 2.55 the no. of tumors/rat in the control groups vs. 0.27 in the treated group. No signs of toxicity were obsd.

TΤ 245036-27-5

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in combination; exemestane as chemopreventing agent for estrogen-dependent cancer)

245036-27-5 CAPLUS RN

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:89818 CAPLUS

DOCUMENT NUMBER:

136:139851

TITLE:

Self-emulsifying drug delivery systems for extremely

water-insoluble, lipophilic drugs

INVENTOR(S):

Gao, Ping; Morozowich, Walter; Shenoy, Narmada Pharmacia + Upjohn Company, USA; Sugen, Inc.

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	KIND DATE					A													
WO 2002007712			A2 20020131					WO 2001-US23140 20010720											
₩:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,			
	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,			
	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,			
	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,			
	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	UŻ,			
	VN,	YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM						
RW:	GH,																		
	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,			
	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG				

PRIORITY APPLN. INFO.:

US 2000-220376P P 20000724

OTHER SOURCE(S):

MARPAT 136:139851

A self-emulsifying drug delivery system for extremely water-insol., lipophilic compds. is disclosed. Self-emulsifying drug delivery systems contg. PVP achieved 10-15% oral bioavailability of 3-[(2,4-dimethylpyrrol-5-yl)methylene]-2-indolinone compared to tablet and oil suspension formulations showing only 0-1% bioavailability.

TT 245036-27-5

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(self-emulsifying drug delivery systems for extremely water-insol.

lipophilic drugs)

RN 245036-27-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

L18 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:868449 CAPLUS

DOCUMENT NUMBER:

136:5902

TITLE:

Preparation of prodrugs of 3-(pyrrol-2-ylmethylidene)-

2-indolinones as modulators of protein-kinase-

activity.

INVENTOR(S):

Moon, Malcolm Wilson; Morozowich, Walter; Gao, Ping;

Koenig, Marcel

PATENT ASSIGNEE(S):

Sugen, Inc., USA; Pharmacia + Upjohn Company

SOURCE:

PCT Int Appl., 123 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:



	PATENT NO.					KIND DATE					APPLICATION NO. DATE							
	wo	2001	0901	03\	A2 20011129			\	Γ	0 20	 01-U	 S167	 41	20010524				
	_	W:	AE,	ĀĠ,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,
			RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	ΤZ,	UA,	UG,	US,
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		RW:	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	ÜĠ,	ZW,	ΑT,	BE,	CH,	CY,
			DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG		
	US	2002	0322	04	A	1	2002	0314		τ	S 20	01-8	6380	4	2001	0524		
	US	2002	0351	40	A	1	2002	0321		ť	S 20	01-8	6390	5	2001	0524		
	US	2002	0378	78	A.	1	2002	0328		τ	S 20	01-8	6381	9	2001	0524		
PRIO	RIT	Y APP	LN.	INFO	.:					US 2	000-	2070	00P	P	2000	0524		
										US 2	000-	2250	45P	P	2000	0811		

OTHER SOURCE(S):

MARPAT 136:5902

GI

Ι

Title compds. [I; R3-R6 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, aryloxy, SH, alkylthio, arylthio, etc.; .gtoreq.2 of R3-R6 = H; R3R4, R4R5, R5R6 = atoms to form aryl ring, OCH2O, OCH2OCH2; R7 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, aryloxy, etc.; R8-R1O = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, aryloxy, SH, arylthio, etc.; Q = CHR11OR21, COR51, OP(O)(ORa)(ORb); R11 = H, alkyl; R21 = H, alkyl, aralkyl, acyl; R51 = alkyl; Ra, Rb = H, alkyl], were prepd. as prodrugs for modulators of protein kinase activity (no data). Thus, 3-(3,5-dimethyl-1H-pyrrol-2-ylmethylidene)-1,3-dihydroindol-2-one was stirred 1 h with aq. H2CO and Et3N in DMF to give (3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylidene]-1-hydroxymethyl-1,3-dihydro-2H-indol-2-one.

RN 210644-62-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & \text{Me} \\ \hline & V & \text{Me} \\ \hline & V & \text{Me} \\ \hline & V & \text{Me} \\ & V & \text{Me} \\ & V & \text{Me} \\ \end{array}$$

L18 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:507531 CAPLUS

DOCUMENT NUMBER:

135:107247

TITLE:

Preparation - heteroarylidenyl-2-indolinone

compounds for modulating protein kinase activity and

for use in cancer chemotherapy

INVENTOR(S):

Langecker, Peter J.; Shawver, Laura K.; Tang, Peng C.;

Sun, Li_

PATENT ASSIGNEE(S):

SOURCE:

Sugen, Inc., USA

PCT Int. Appl., 93 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
                                                            DATE
    WO 2001049287 A1 20010712
                                           WO 2000-US18058 20000630
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                         WO 1999-US31232 19991230
    WO 2000038519
                      A1
                            20000706
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             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        US 1999-476232
                                                            19991230
                                        WO 1999-US31232
                                                            19991230
                                                         Α
                                        US 2000-569545
                                                         A
                                                            20000512
                                        US 1998-114313P
                                                         P
                                                            19981231
```

OTHER SOURCE(S):

MARPAT 135:107247

$$\begin{array}{c|cccc}
R4 & C-R3 \\
R5 & R7 & R1 \\
R7 & R1 & I
\end{array}$$

The present invention relates to 3-heteroarylidenyl-2-indolinone compds. AΒ [I; R1 = H, alkyl; R2 = O, S; R3 = H; R4, R5, R6, R7 = H, alkyl, alkoxy, aryl, aryloxy, alkaryloxy, halo, trihalomethyl, S(O)R, SO2NRR', SO3R, SR, NO2, NRR', OH, cyano, COR, O2CR, (CH2)nCO2R, CONRR'; A = a five membered heteroaryl selected from (un) substituted thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, 2-sulfonylfuran, 4-alkylfuran, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, etc.; n = 0-3; R, R' = H, alkyl, aryl] or physiol. acceptable salts or prodrugs thereof are prepd. These compds. modulate the enzymic activity of protein kinases such as receptor protein tyrosine kinase, cellular tyrosine kinase, and serine threonine kinase and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer. Furthermore, these compds. are expected to enhance the efficacy of other chemotherapeutic agents, in particular, fluorinated pyrimidines, in the treatment of cancer. In a cellular-based assay for inhibiting the receptor phosphorylation, 3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-2indolinone (II) inhibited Flk-1-autophosphorylation with IC50 of .apprx.1 .mu.M. II in vitro inhibited proliferation of endothelial cells induced

by VEGF with IC50 of .apprx.0.07 .mu.M. Although II in vitro had no direct inhibitory effect on a variety of tumor cell lines at concn. up to 50 .mu.M, it in vivo demonstrated a significant suppression of tumor growth against a broad spectrum of tumor types s.c. implanted into immunocompromised mice and whose growth are driven by various growth factors such as PDGF, EGF, and Her2.

ΙT 245036-27-5P

CN

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-heteroarylidenyl-2-indolinone compds. for modulating protein kinase activity for cancer chemotherapy)

245036-27-5 CAPLUS RN

> 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm O}$ $^{\rm H}_{
m N}$ $^{\rm Me}$ $^{\rm CH}_2$ $^{\rm CH}_2$ $^{\rm CO}_2$ $^{\rm H}$

REFERENCE COUNT:

8 THERE ARE 8 CITED REFERENCES-AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L18 ANSWER 5 OF 16 ACCESSION NUMBER: 2001:472477 CAPLUS

DOCUMENT NUMBER:

135:56059

TITLE:

Methods of modulating c-kit tyrosine protein kinase

function with indolinone compounds

INVENTOR(S):

Lipson, Ken; McMahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE -----WO 2001045689 __A2_ 20010628 WO 2000-US35009 20001222 WO 2001045689 A3 20020103 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002010203 20020124 US 2000-741842 A1 20001222 PRIORITY APPLN. INFO.: US 1999-171693P P 19991222 MARPAT 135:56059

OTHER SOURCE(S):

AB The invention concerns indolinone compds. and their use to inhibit the activity of a receptor tyrosine kinase. The invention is preferably used to treat cell proliferative disorders such as cancers characterized by over-activity or inappropriate activity of c-kit kinase.

IT 245036-27-5 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(indolinone derivs. for c-kit tyrosine protein kinase function modulation)

RN 245036-27-5 CAPLUS

> 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$H$$
 CH
 H
 N
 Me
 $CH_2-CH_2-CO_2H$

L18 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:396655 CAPLUS

DOCUMENT NUMBER:

135:19549

TITLE:

CN

Preparation of pyrrole substituted 2-indolinones Shenoy, Narmada; Sorasuchart, Waranush Sugena, Inc., USA

INVENTOR(S):

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 249 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

GΙ

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO. KII					ND DATE APPLICATION N							٥.	DATE				
	2001 2001				20010531 WO 2000-US32277 3 20011213								77	20001122				
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
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														LK,				
														PL,	-	-		
		SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	
		YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM					
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
PRIORITY	APP	LN.	INFO	. :				I	US 19	999-	1675	44P	A1	1999	1124	•		
OTHER SC	URCE	(S):			MAR	PAT :	135:	1954	9									

The title compds. [I; R1 = H, alkyl, alkenyl, etc.; R2 = H, halo, alkyl, etc.; R3-R6 = H, alkyl, trihaloalkyl, etc.; R3 and R4, R4 and R5, R5 and R6 may combine to form a six membered aryl ring, OCH2O, OCH2CH2O; R7 = H, alkyl, cycloalkyl, etc.; R8-R10 = H, alkyl, trihaloalkyl, etc.] were prepd. and formulated. E.g., a multi-step synthesis of I [R1-R7 = H; R8, R10 = Me; R9 = (CH2)2CO2H] which showed 79-86% inhibition of tumor growth of Calu-6 cells in mice at 75 and 100 mg/kg/day, was given. The present invention features formulations of indolinones which compds. are ionizable as free acids or free bases. The formulation is suitable for parenteral or oral administration, wherein the formulation comprises an ionizable substituted indolinone, and a pharmaceutically acceptable carrier.

The term whom able substituted indolinone includes pyrrole substituted 2-indolinones I which, in addition to being otherwise optionally substituted on both the pyrrole and 2-indolinone portions of the compd., are necessarily substituted on the pyrrole moiety with one or more hydrocarbon chains which themselves are substituted with at least one polar group.

IT 245036-27-5P

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)

(prepn. of pyrrole substituted 2-indolinones as antitumor agents)

RN 245036-27-5 CAPLUS

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm O}_{
m CH}$ $^{\rm H}_{
m N}$ $^{\rm Me}_{
m CH_2-CH_2-CO_2H}$

IT 251356-54-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyrrole substituted 2-indolinones as antitumor agents)

RN 251356-54-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, monosodium salt (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm O}_{
m CH}$ $^{\rm H}_{
m N}$ $^{\rm Me}$ $^{\rm CH}_2$ $^{\rm CH}_2$ $^{\rm CO}_2$ $^{\rm H}$

Na

L18 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:456819 CAPLUS

DOCUMENT NUMBER:

133:84238

TITLE:

3-heteroarylidenyl-2-indolinone compounds for

modulating protein kinase activity and for use in

cancer chemotherapy

INVENTOR(S):

Langecker, Peter J.; Shawver, Laura Kay; Tang, Peng

Cho; Sun, Li

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

2

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                     KIND
                           DATE
                                          APPLICATION NO.
                                                           DATE
                     ____
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     W@#2000038519
                      A1
                           20000706---
                                         WO 1999-US31232 19991230
            AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
            TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                     BR 1999-16735
     BR 9916735
                           20010925
                      Α
     EP 1139754
                                         EP.-1.999-966725
                      A1
                           20011010
                                                          49991230
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
            IE, SI, LT, LV, FI, RO
    WO 2001049287
                     A1 20010712
                                          WO 2000-US18058 20000630
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
            CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
            ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
            LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
            ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
            CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                       US 1998-114313P
                                                        Ρ
                                                           19981231
                                       US 1999-476232
                                                        Α
                                                           19991230
                                       WO 1999-US31232
                                                        W
                                                           19991230
                                       US 2000-569545
                                                        Α
                                                           20000512
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OTHER SOURCE(S): MARPAT 133:84238

3-Heteroarylidenyl-2-indolinone compds. are provided that modulate the enzymic activity of protein kinases and therefore are expected to be

useful in the prevention and treatment of protein kinase-related cellular disorders, e.g. cancer. Furthermore, these compds. are expected to enhance the efficacy of other chemotherapeutic agents, in particular, fluorinated pyrimidines, in the treatment of cancer.

245036-27-5

TΤ

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(heteroarylidenylindolinone derivs. for modulating protein kinase activity and in cancer chemotherapy)

RN 245036-27-5 CAPLUS

> 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L18 ANSWER 8 OF 16 1999:764021 CAPLUS

ACCESSION NUMBER:

Patent

English-

DOCUMENT NUMBER: TITLE:

132:12257

Preparation of pyrrole substituted 2-indolinone protein kinase inhibitors

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 240 pp.

CODEN: PIXXD2

Sugen, Inc., USA

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. ĎAŢE KIND APPLICATION NO. DATE 19991202 A1 WO 1999-US12069 19990528 ĂĹ, ΑM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, GA, GN, GW, ML, MR, NE, SN, TD, TG CI, CM, CA 2314156 AΑ **-19991202** CA 1999-2314156 19990528 AU 1999-44102 AU 9944102 Α1 19991213 19990528 EP 1082305 EP 1999-927120 Α1 20010314 19990528 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, SI, LT, LV, FI, RO

BR 9910792 Α 20020129 BR 1999-10792 19990528 NO 2000-5916_ 20001122

19990528

NO 2000005916 Α 20010129 PRIORITY APPLN. INFO.:

US 1998-87310P 19980529 US 1999-116106P **~** P 19990115

WO 1999-US12069

OTHER SOURCE(S): MARPAT 132:12257 GI

The present invention relates to 5-(2-oxo-1,2-dihydroindol-3-AB ylidenemethyl)-1H-pyrrol-3-ylalkanoic acid derivs. (I) [where R1 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl, OH, alkoxy, carboxy, acetyl, (thio)amido, (trihalomethane)sulfonyl, etc.; R2 = H, halo, (cyclo)alkyl, (hetero)aryl, or heteroalicyclic; R3, R4, R5, R6, R8, R9, R10 = independently H, (cyclo)alkyl, trihaloalkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heteroalicyclic, OH, alkoxy, SH, alkylthio, arylthio, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxy, amido, CN, NO2, halo, (thio)carbamyl, (un)substituted amino, etc.] which modulate the activity of protein kinases and are useful in the prevention and treatment of protein kinase related cellular disorders, such as cancer. 2,4-dimethyl-5-ethoxycarbonyl-3-(2-ethoxycarbonylethyl)pyrrole was deprotected using NaOH to form 3-(2-carboxyethyl)-2,4-dimethylpyrrole (100%) and the product C-5 formylated (two methods given for 86% and 90% yield, resp.). Reaction with 2-oxindole in EtOH and pyrrolidine or in aq. NaOH yielded II (88% and 91%, resp.), which reduced the av. size of C6 human glioma and melanoma tumors s.c. implanted in mice by 80-85%. II, when administered orally, demonstrated notably superior efficacy compared to structurally similar analogs.

Ι

II

245036-27-5P 251356-54-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; prepn. of 5-(2-oxo-1,2-dihydroindol-3-ylidenemethyl)-1H-pyrrol-3-ylalkanoic acid protein kinase inhibitors as antitumor agents)

RN 245036-27-5 CAPLUS

IT

CN

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
 $^{\rm CH}$ $^{\rm Me}$ $^{\rm CH_2-CH_2-CO_2H}$

RN251356-54-4 CAPLUS

> 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, monosodium salt (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O \\ \hline H & Me \\ \hline CH & Me \\ \hline Me & CH_2-CH_2-CO_2H \\ \hline \end{array}$$

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS

5

ACCESSION NUMBER:

1999:626172 CAPLUS

DOCUMENT NUMBER:

131:257441

TITLE:

CN

Heterocyclic families of compounds [tricyclic-based

indolinones and pyrazolecarboxylic acid amides] for

the modulation of tyrosine protein kinase

INVENTOR(S):

Fong, Annie; Hannah, Alison; Harris, David G.; Hirth, Peter; Hubbard, Steven R.; Langecker, Peter; Liang,

Congxin; McMahon, Gerald; Mohammadi, Moosa; Schlessinger, Joseph; Shawver, Laura K.; Sun, Li;

Tang, Peng C.; Ullrich, Axel

PATENT ASSIGNEE(S):

Sugen, Inc., USA; New York University; Max-Planck

Institut fur Biochemie

SOURCE:

PCT Int. Appl., 269 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.		KI	ND	DATE			A	PPLI	CATI	N NC	٥.	DATE			
WO 9948	A2 19990930 A3 20000224					WO 1999-US6468 19990326										
₩:	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
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	KΡ,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN.	MW.	MX.
	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR.	TT.
	UA,	UG,	US,	UZ,	VN,	YU,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ.	TM
RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY.	DE.	DK.
	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,
	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG	·	·	•	•	

Page 15

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19990930
    CA 2325935
                     AA
                                         CA 1999-2325935 19990326
                          19991018
    AU 9933635
                     Α1
                                         AU 1999-33635
                                                        19990326
                           20010110
    EP 1066257
                     Α2
                                         EP 1999-915018 19990326
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
                           20020312
    JP 2002507598
                      T2
                                         JP 2000-537851
                                                         19990326
PRIORITY APPLN. INFO.:
                                      US 1998-79713P P 19980326
                                      US 1998-80422P
                                                      P 19980402
                                      US 1998-81792P P 19980415
                                      US 1998-82056P P 19980416
                                      US 1998-89397P P 19980615
                                      US 1998-89521P
                                                     P 19980616
                                      US 1998-98783P
                                                     P 19980901
                                      WO 1999-US6468
                                                     W 19990326
OTHER SOURCE(S):
                       MARPAT 131:257441
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention relates to certain indolinone-based and pyrazolylamide-based compds., I and II, their method of synthesis, and combinatorial libraries ΑB consisting of the compds. [wherein AB = atoms to make up 1-2 fused and/or connected rings; R = arom. or heteroarom. ring which may form an addnl. ring by cyclization to the methylene group; R1, R2 = H, alkyl, (hetero)aryl or -aliph. ring, amino, NO2, halo, etc.; R3 = (un)substituted Ph; Z = (un) substituted (CH2)0-3; R4, R5 = H, alkyl, (hetero)aryl or -aliph., amine, ketone, etc.]. The invention also relates to methods of modulating the function of protein kinases using these compds., and methods of treating diseases by modulating the function of protein kinases and related signal transduction pathways. Data for prepns. and/or biol. activity are given, as well as the prepns. of various oxindole intermediates. For instance, the pyrazolecarboxamide deriv. III gave up to 70% inhibition of growth of Calu-6 human lung carcinoma cells as a xenograft in mice. As another example, the indolinone deriv. IV was prepd. by condensation of 6-(4-methoxyphenyl)-2-oxindole with 3,5-dimethyl-1H-pyrrole-2-carboxaldehyde in the presence of piperidine. Extensive tests of a few selected compds. against a variety of protein kinases are described.

IT 245036-27-5P, 3-[2,4-Dimethyl-5-[(2-oxo-1,2-dihydroindol-3ylidene)methyl]-1H-pyrrol-3-yl]propionic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; prepn. of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators) 245036-27-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN

Page 16

L18 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:757553 CAPLUS

DOCUMENT NUMBER:

132:137242

TITLE:

Design, Synthesis, and Evaluations of Substituted

3-[(3- or 4-Carboxyethylpyrrol-2-

yl)methylidenyl]indolin-2-ones as Inhibitors of VEGF,

FGF, and PDGF Receptor Tyrosine Kinases

AUTHOR(S):

SOURCE:

Sun, Li; Tran, Ngoc; Liang, Congxin; Tang, Flora;

Rice, Audie; Schreck, Randall; Waltz, Kara; Shawver,

Laura K.; McMahon, Gerald; Tang, Cho

CORPORATE SOURCE:

SUGEN Inc., South San Francisco, CA, 94080-4811, USA

Journal of Medicinal Chemistry (1999), 42(25),

5120-5130

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE: English

Receptor tyrosine kinases (RTKs) were implicated as therapeutic targets for the treatment of human diseases including cancers, inflammatory diseases, cardiovascular diseases including arterial restenosis, and fibrotic diseases of the lung, liver, and kidney. Three classes of 3-substituted 2-indolinones contg. propanoic acid functionality attached to the pyrrole ring at the C-3 position of the core were identified as catalytic inhibitors of the vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF) RTKs. Some of the compds. were found to inhibit the tyrosine kinase activity assocd. with isolated vascular endothelial growth factor receptor 2 (VEGF-R2) [fetal liver tyrosine kinase 1 (Flk-1)/kinase insert domain-contg. receptor (KDR)], fibroblast growth factor receptor (FGF-R), and platelet-derived growth factor receptor (PDGF-R) tyrosine kinase with IC50 values at nanomolar level. Thus, SU 5402 [5-[(1,2-dihydro-2-oxo-3Hindol-3-ylidene)methyl]-4-methyl-1H-Pyrrole-3-propanoic acid] showed inhibition against VEGF-R2 (Flk-1/KDR) and FGF-R1 tyrosine kinase activity with IC50 values of 20 and 30 nM, resp., while 5-[(1,2-dihydro-2-oxo-6phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-propanoic acid inhibited the PDGF-R tyrosine kinase activity with IC50 value of 10 nM. Structural models and structure-activity relationship anal. of these compds. for the target receptors are discussed. The cellular activities of these compds. were profiled using cellular proliferation assays as measured by bromodeoxyuridine (BrdU) incorporation. Specific and potent inhibition of cell growth was obsd. for some of these compds. These data provide evidence that these compds. can be used to inhibit the function of these target receptors.

245036-27-5P, 5-[(1,2-Dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4dimethyl-1H-Pyrrole-3-propanoic acid

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and evaluation of [(dihydrooxoindolylidene)methyl]pyrrolepropan oic acid as tyrosine kinase inhibitors)

RN 245036-27-5 CAPLUS

CN

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS 15 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 16 USPATFULL

ACCESSION NUMBER:

2002:17323 USPATFULL

TITLE:

Methods of modulating c-kit tyrosine protein kinase

function with indolinone compounds

INVENTOR(S):

Lipson, Ken, San Mateo, CA, UNITED STATES McMahon, Gerald, Kenwood, CA, UNITED STATES

KIND NUMBER DATE -----US 2002010203 A1 20020124 PATENT INFORMATION: US 2000-741842 A1 20001222 (9) APPLICATION INFO.:

> NUMBER DATE

PRIORITY INFORMATION:

US 1999-171693P Utility 19991122/(60)

DOCUMENT TYPE:

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

John P. Isacson, FOLEY & LARDNER, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: NUMBER OF DRAWINGS:

2 Drawing Page(s)

LINE COUNT:

1762

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention concerns compounds and their use to inhibit the activity of a receptor tyrosine kinase. The invention is preferably used to treat cell proliferative disorders such as cancers characterized by over-activity or inappropriate activity c-kit kinase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 245036-27-5

(indolinone derivs. for c-kit tyrosine protein kinase function modulation)

RN 245036-27-5 USPATFULL

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

 $\mathrm{CH_2}-\mathrm{CH_2}-\mathrm{CO_2H}$ Me

Answers 12-16 are très bizane. I've

L18 ANSWER 12 OF 16 USPATFULL

ACCESSION NUMBER:

PATENT ASSIGNEE(S):

TITLE:

INVENTOR(S):

NUMBER

corporation)

KIND

2001:83308 USPATFULL

Monolithic 3D radial powe
Stones, David I., Torranc
Lee, Alfred E., Torrance,
TRW Inc., Redondo Beach,
corporation

acommon ?-

Searched by Barb O'Bryen, STIC 308-4291

PATENT INFORMATION:

ÚS 6242984 / US 1998-80422

В1 20010605

APPLICATION INFO.: DOCUMENT TYPE:

Utility

19980518 (9)

FILE SEGMENT: PRIMARY EXAMINER:

Granted Lee, Benny

LEGAL REPRESENTATIVE:

Yatsko, Michael S.

NUMBER OF CLAIMS:

26

EXEMPLARY CLAIM:

1,2,3,4

NUMBER OF DRAWINGS:

4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An SSPA module in accordance with the present invention comprises a signal input (102), and a radfal splitter (100) connected to the signal input (102) comprising a plurality of radially extending splitter waveguides 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126. The SSPA module also includes a signal output (202), and a radial combiner (200) connected to the signal output (202) comprising a plurality of radially extending combiner waveguides 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226. Connections between the splitter (100) and combiner (200) are provided by a plurality of vertically extending waveguides 404, 406, 408, 410, 412, 414, 416, 418, 420, 422, 424, 426. The SSPA module also includes a plurality of processing circuits 304, 308, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, for example MMIC amplifiers, connected to the combiner waveguides 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226. A waveguide to microstrip transition (510) may also be used to connect signals propagating in the waveguides to and from microstrip lines connected to the processing circuitry (304-326). Generally, the transition (510) includes a waveguide section (512) with a top conducting layer (516) that defines a first slit (526) and a second slit (528) bounding a transition area (530) abutting a microstrip section (514) to form a waveguide to microstrip transition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

245036-27-5P, 3-[2,4-Dimethyl-5-[(2-oxo-1,2-dihydroindol-3-

ylidene)methyl]-1H-pyrrol-3-yl]propionic acid

(target compd.; prepn. of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators)

RN 245036-27-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
 $^{\rm CH}$ $^{\rm CH}$ $^{\rm Me}$ $^{\rm CH}_2-{\rm CH}_2-{\rm CO}_2{\rm H}$

L18 ANSWER 13 OF 16 USPATFULL

ACCESSION NUMBER:

2001:15039 USPATFULL

TITLE:

Variable delay circuit and semiconductor intergrated

circuit device

INVENTOR(S):

Yamazaki, Masafumi, Kawasaki, Japan

Tomita, Hiroyoshi, Kawasaki, Japan

PATENT ASSIGNEE(S):

Fujitsu Limited, Kawasaki, Japan (non-U.S. corporation)

NUMBER KIND DATE PATENT INFORMATION: APPLICATION INFO.: US 6181184 US 1998-89397 B1 20010130 19980603 (9)

NUMBER DATE ------

PRIORITY INFORMATION:

JP 1997-203315

19970729

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER:

Cunningham, Terry D.

ASSISTANT EXAMINER:

Tra, Quan

LEGAL REPRESENTATIVE:

Armstrong, Westerman, Hattori, McLeland, & Naughton

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

46 Drawing Figure (s); 44 Drawing Page(s)

LINE COUNT:

2911

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A variable delay circumtaincludes a load on a signal transfer line, at least one transistor connected to the signal transfer line. Each transistor is controlled by a gate voltage thereof so that a signal on the signal transfer line is delayed in response to a magnitude of the gate capacitance connected thereto.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

245036-27-5P, 3-[2,4-Dimethyl-5-[(2-oxo-1,2-dihydroindol-3-

ylidene)methyl]-1H-pyrrol-3-yl]propionic acid

(target compd.; prepn. of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators)

RN 245036-27-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$H$$
 CH
 H
 Me
 $CH_2-CH_2-CO_2H$

L18 ANSWER 14 OF 16 USPATFULL

ACCESSION NUMBER:

2000:90153 USPATFULL

TITLE:

System for automatic inspection and ejection of cartons

in a packaging machine

INVENTOR(S):

Robinson, Glenn, Alpharetta, GA, United States

Potteiger, Thomas M., Powder Springs, GA, United States

Jacob, Jeffrey G., Gainesville, GA, United States

PATENT ASSIGNEE(S): The Mead Corporation, Dayton, OH, United States (U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION:

US 6088995 US 1998-98783 20000718 19980**@**7

APPLICATION INFO.: DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Coan, James F. Drew, Michael V.

NUMBER OF CLAIMS:

4

EXEMPLARY CLAIM: NUMBER OF DRAWINGS:

13 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT:

355

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A system for automatic inspection and ejection of cartons in a packaging AB machine includes detection elements (20, 22) for determining whether a carton (C) has assumed a predetermined configuration at a predetermined point in its path of travel. Carton ejection elements include rollers (30, 32) which are actuated to eject a carton (C) when the detection elements (20) determine that the carton has not assumed the predetermined configuration at the predetermined point in its path of travel. A synchronous relationship between a flow of cartons (C) and a flow of groups of articles (G) to be packaged is preserved at and as cartons leave the carton inspection and ejection station of a packaging machine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

245036-27-5P, 3-[2,4-Dimethyl-5-[(2-oxo-1,2-dihydroindol-3-

ylidene)methyl]-1H-pyrrol-3-yl]propionic acid

(target compd.; prepn. of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators)

RN 245036-27-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

L18 ANSWER 15 OF 16 USPATFULL

ACCESSION NUMBER:

TITLE:

2000:79392 USPATFULL

Valve-timing controller for an internal combustion engine

INVENTOR(S):

Morikawa, Junya, Toyota, Japan

PATENT ASSIGNEE(S): Denso Corporation, Japan (non-U.S. corporation)

	 NUMBER	KIND	DATE	
PATENT INFORMATION INFO	 6079381 1998-81792		20000627 19980520	(9)

NUMBER DATE PRIORITY INFORMATION:

DOCUMENT TYPE:

JP 1997-131341 19970521

Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Lo, Weilun LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 21

Nixon & Vanderhye PC

EXEMPLARY CLAIM: 1 NUMBER OF DRAWINGS:

18 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT:

734

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A system and method for determining abnormality of a VVT (variable valve-timing control mechanism) and controlling the VVT on consideration of responsiveness thereof. When execution conditions for abnormality determination of the VVT are present, speed of change in angle of rotation ACSPD is calculated on a basis of transition in actual angle of

rotation of the VVT as a responsiveness-detection parameter. In the abnormality determination, if the speed of change in angle of rotation ACSPD is less than a programmed determination value, it is determined that followup of VVT operation is faulty, and an abnormality-determination flag XVTFAIL is set to "1" to indicate that some abnormality has occurred. Also, a warning light is placed in an illuminated state. Target relative angle of rotation of the VVT is appropriately established, and VVT operation is suppressed on the basis of this abnormality determination. As a result, drivability and emissions performance degradation can be suppressed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 245036-27-5P, 3-[2,4-Dimethyl-5-[(2-oxo-1,2-dihydroindol-3-

ylidene)methyl]-1H-pyrrol-3-yl]propionic acid

(target compd.; prepn. of pyrazolecarboxylic acid amides and (arylmethylene)indolinones as protein tyrosine kinase modulators)

RN 245036-27-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

L18 ANSWER 16 OF 16 USPATFULL

ACCESSION NUMBER: 2000:6506 USPATFULL

TITLE:

Fabric supporting ring fixtures for creating bed canopy

and window drapery arrangements

INVENTOR(S):

Harkinson, Greg, 12121 Veterans Memorial Dr., Ste. 2,

Houston, TX, United States 77067

NUMBER KIND DATE ______ PATENT INFORMATION: US 6015004 20000118 APPLICATION INFO.: US 1998-87310 19980529 (9) DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Purol, David M. Roddy, Kenneth A. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 9 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Figure(s); 6 Drawing Page(s)

LINE COUNT: 465

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fabric supporting ring fixtures for use in creating bed canopy and window drapery arrangements. A corner ring fixture has a central body portion configured to be supported in a first plane from a support surface and a pair of fabric receiving ring elements each having an outer circumferential portion extending outwardly from the central body portion in a second plane different from the first plane. An intermediate ring fixture has a central body portion configured to be supported from a support surface and a fabric receiving ring element with an outer circumferential portion extending perpendicularly outward therefrom. The fabric receiving ring elements have a central circular opening sized to pass fabric and drapery materials therethrough and to support the fabric and drapery materials in decorative arrangements.

Typically, the corner ring fixtures are installed on a flat surface above a bed or window in spaced apart relation and allow a length of fabric material to be passed through its ring elements to selectively make a transition from a first horizontal plane to a second horizontal plane angularly offset therefrom or to make a transition from a horizontal plane to a vertical plane, and the intermediate ring fixtures are installed on a flat surface between the spaced apart corner ring fixtures to support lengths of fabric material passed through the corner ring fixtures.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 245036-27-5P 251356-54-4P

(target compd.; prepn. of 5-(2-oxo-1,2-dihydroindol-3-ylidenemethyl)-1H-pyrrol-3-ylalkanoic acid protein kinase inhibitors as antitumor agents)

RN 245036-27-5 USPATFULL CN 1H-Pvrrole-3-propanoic

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & Me & CH_2-CH_2-CO_2H \\ \hline \end{array}$$

RN 251356-54-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, monosodium salt (9CI) (CA INDEX NAME)

Na

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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L19

0 L15

Jones 09/716332 Page 24

=> fil capl; d que nos 144; d que nos 145; s (144 or 145) not 116 FILE 'CAPLUS' ENTERED AT 14:53:38 ON 30 APR 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 30 Apr 2002 VOL 136 ISS 18 FILE LAST UPDATED: 29 Apr 2002 (20020429/ED)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L27
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L30
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L44
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L60
                 L29)
                                                                               PAC-pharmacological activity

PAC-pharmacological activity

PKT-pharmacological DMA-drug mechanism
of action
             41 (L44 OR L59 OR L60) NOT (L16) previously
L63
=> fil uspatf; d que nos 156
FILE 'USPATFULL' ENTERED AT 15:01:48 ON 30 APR 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 25 Apr 2002 (20020425/PD)
FILE LAST UPDATED: 25 Apr 2002 (20020425/ED)
HIGHEST GRANTED PATENT NUMBER: US6378132
HIGHEST APPLICATION PUBLICATION NUMBER: US2002049999
CA INDEXING IS CURRENT THROUGH 25 Apr 2002 (20020425/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 25 Apr 2002 (20020425/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2002
>>> USPAT2 is now available. USPATFULL contains full text of the
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     original, i.e., the earliest published granted patents or
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     applications. USPAT2 contains full text of the latest US
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     publications, starting in 2001, for the inventions covered in
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     USPATFULL. A USPATFULL record contains not only the original
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     published document but also a list of any subsequent
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     publications. The publication number, patent kind code, and
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>>> publication date for all the US publications for an invention
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     are displayed in the PI (Patent Information) field of USPATFULL
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     records and may be searched in standard search fields, e.g., /PN,
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     /PK, etc.
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>>> USPATFULL and USPAT2 can be accessed and searched together
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     through the new cluster USPATALL. Type FILE USPATALL to
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     enter this cluster.
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    Use USPATALL when searching terms such as patent assignees,
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     classifications, or claims, that may potentially change from
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     the earliest to the latest publication.
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This file contains CAS Registry Numbers for easy and accurate
substance identification.
T.4
                 STR
L7
            771 SEA FILE=REGISTRY SSS FUL L4
T.46
            336 SEA FILE=REGISTRY ABB=ON L7 AND USPATFULL/LC
1.47
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L48
           6553 SEA FILE=USPATFULL ABB=ON
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L50
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L51
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L52
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L53
         117125 SEA FILE-USPATFULL ABB-ON AIDS OR HIV OR (ACQUIRED OR
                 HUMAN) (W) (IMMUNE DEFICIEN? OR IMMUNODEFICIEN?)
L54
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31 SEA FILE=USPATFULL ABB=ON L47 AND L48 AND (L49 OR L50 OR L51

OR L52 OR L53 OR L54)

L56

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=> s 156 not 117
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=> dup rem 163,164
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CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L64
             70 DUP REM L63 L64 (1 DUPLICATE REMOVED)
L65
                ANSWERS '1-41' FROM FILE CAPLUS
                ANSWERS '42-70' FROM FILE USPATFULL
=> d ibib abs hitstr 165 1-70; fil hom
L65 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2002 ACS
                                                       DUPLICATE 1
                         2000:622463 CAPLUS
ACCESSION NUMBER:
                         133:217719
DOCUMENT NUMBER:
TITLE:
                         3-(Cyclohexanoheteroarylidenyl)-2-indolinone
                         protein tyrosine kinase inhibitors,
                         and their therapeutic use
                         Tang, Peng Cho; Sun, Li; McMahon, Gerald; Blake,
INVENTOR(S):
                         Robert A.
                         Sugen, Inc., USA
PATENT ASSIGNEE(S):
                         U.S., 61 pp., Cont. -in-part of U.S. Ser. No. 99,842.
SOURCE:
                         CODEN: USXXAM
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                           APPLICATION NO.
                                                           DATE
                      KIND
                            DATE
                                            _____
                                                            _____
                       A 20000905
                                           US 1998-190970 19981112
     US 6114371
     US 6130238
                            20001010
                                           US 1998-99842
                                                            19980619
                                        US 1997-50977P
                                                        P
                                                            19970620
PRIORITY APPLN. INFO.:
                                        US 1997-59384P
                                                         P 19970919
                                        US 1998-99842
                                                         A2 19980619
                                        US 1997-59544P
                                                         P 19970919
                         CASREACT 133:217719; MARPAT 133:217719
OTHER SOURCE(S):
     3-(Cyclohexano-heteroarylidenyl)-2-indolinone compds., and physiol.
     acceptable salts and prodrugs thereof, are disclosed which are expected to
     modulate the activity of protein tyrosine kinases and
     therefore to be useful in the prevention and treatment of protein
     tyrosine kinase-related cellular disorders (cancer,
     arthritis, restenosis, etc.).
TΤ
     245035-93-2 245036-08-2 245036-22-0
     290821-16-8
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclohexanoheteroarylidenyl indolinone protein tyrosine
        kinase inhibitors, and therapeutic use)
RN
     245035-93-2 CAPLUS
     2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-
CN
     methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)
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RN 245036-08-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 245036-22-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 290821-16-8 CAPLUS

CN 2H-Indol-2-one, 6-bromo-1,3-dihydro-3-[(4,5,6,7-tetrahydro-3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 2 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:220379 CAPLUS

DOCUMENT NUMBER:

136:268137

TITLE:

Use of arginine in the preparation of a medicament for the prevention and treatment of the side effects associated with the intravenous administration of

pharmaceuticals

Searched by Barb O'Bryen, STIC 308-4291

Page 28

Muggetti, Lorena; Martini, Alessandro; Buzzi, Giovanni; Colombo, Paolo

PATENT ASSIGNEE(S): Pharmacia & Upjohn S.p.A., Italy

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR(S):

	PAT	ENT	NO.		KI	ND	DATE			APPLICATION NO. DATE								
	WO	2002	0221	34	A1 20020321				W	20	01-E	P103	98	2001	0907			
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			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
															NO,			
			RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,
															TJ,			
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,
			DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
PRIO	RITY	APP	LN.	INFO	.:					IT 2	000-1	MI19	84	Α	2000	0912		
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	par	ticu	lar,	to ·	the	inje	ctab	le f	ormu.	latio	ons.	for	1V	use	Com	oris	ing.	it, in
	the	pre	vent	ion a	and	trea	tmen	t of	the	sid	e.ef	fect	s as	socc	wi	th tl	ne	nustine
	exť	rava	sati	on_o	f dr	ugs	admi	nist	ered	by_	iv	-rou	te.	A s	alt o	of e	stra	nustine
	pho	spha	te w	ith	argi	nine	was	pre	öd.			•						
ΙT	-	005-			_													

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (arginine in prepn. of a medicament for prevention and treatment of side effects assocd. with i.v. administration of pharmaceuticals)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 3 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:31440 CAPLUS

DOCUMENT NUMBER: 136:10238

TITLE: Preparation and use of 4-heteroaryl-3-heteroarylidenyl-

2-indolinones and their use as protein

kinase inhibitors

INVENTOR(S): Tang, Peng Cho; Wei, Chung Chen; Huang, Ping; Cui,

Jingron

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: PCT Int. Appl., 164 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                        KIND
                              DATE
                                               APPLICATION NO.
                                                                 DATE
                              20020110 WO 2001-US20768
     WO 2002002551_
                        _A1_
                                                                 20010629
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                      AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
              RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
              UZ, VN,
                      YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                           US 2000-215654P P 20000630
OTHER SOURCE(S):
                           MARPAT 136:102386
GΙ
```

AB Title compds. I [R1-2 = H, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, etc.; Het = (un) substituted arom. heterocycle contg. at least one and not more than two N atoms, tetrahydro(thio)pyranyl, (thio)morpholino, piperidinyl, piperazinyl, tetrazolyl, etc.; Q = (un)substituted arom. heterocycle contg. not more than two N atoms, 5-membered ring (un) substituted heterocycle contg. N, O or S, e.g., imidazolyl, pyrrolyl, indolyl, etc.] with some exceptions, were prepd. Included are 75 synthetic examples and results for several protein tyrosine kinase assays for those compds. For instance, 4-bromoindole was coupled to bis(pinacolato)diborane (DMSO, KOAc, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 22 h). The resulting dioxaborolane was coupled to 4-bromopyridine.bul.HCl (THF, Pd(PPh3)4, NaOH, 70.degree.C, 6 h) to give the indole which was treated with C5H5N.bul.Br3 (t-BuOH/EtOH/H2O, 1h) followed by zinc (stirred 1 addnl. hour) to give 4-(pyridin-4-yl)-1,3-dyhydroindol-2-one as a yellow solid. Condensation of this intermediate with 5-methylimidazole-4-carboxaldehyde (EtOH, piperidine, 2 days) afforded II. II had IC50 = 4.88 mM for FGFR-1 tyrosine kinase and 0.03 mM for cdk2/cyclin A tyrosine kinase. I are useful in treating cancer, immunol. disorders, etc.

IT 388116-44-7P 388116-47-0P 388116-50-5P 388116-51-6P 388116-52-7P 388116-54-9P 388116-55-0P 388116-56-1P 388116-57-2P, 3-(1H-Indol-2-ylmethylene)-4-(pyridin-4-yl)-1,3-dihydroindol-2-one 388116-60-7P 388116-61-8P 388116-64-1P 388116-65-2P 388116-66-3P 388116-68-5P 388116-73-2P 388116-74-3P 388116-76-5P 388116-80-1P, 3-[3-Methyl-4-((piperidin-1-yl)carbonyl)pyrrol-2-ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one 388116-81-2P, 3-[3-Methyl-4-(morpholine-4-carbonyl)pyrrol-2-ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one 388116-86-7P, 3-(3,5-Dimethyl-1H-pyrrol-2-ylmethylene)-4-

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(piperidin-4-yl)-1,3-dihydroindol-2-one 388116-87-8P
388116-88-9P 388116-89-0P 388116-90-3P
388116-91-4P 388116-92-5P 388116-93-6P,
3-(1H-Indol-2-ylmethylene)-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
388116-96-9P 388116-97-0P 388116-99-2P
388117-00-8P, 3-[(3-Methyl-5-(4-methylpiperazin-1-
ylcarbonyl)pyrrol-2-yl)methylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-
one 388117-01-9P 388117-02-0P 388117-05-3P
388117-06-4P 388117-07-5P 388117-08-6P
388117-10-0P 388117-12-2P 388117-14-4P
388117-16-6P, 3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-
ylcarbonyl)pyrrol-2-yl)methylene]-4-pyridin-2-yl-1,3-dihydroindol-2-one
388117-17-7P, 3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-
ylcarbonyl)pyrrol-2-yl)methylene]-4-pyrimidin-5-yl-1,3-dihydroindol-2-one
388117-18-8P, 3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-
ylcarbonyl)pyrrol-2-yl)methylene]-4-(thiazol-2-yl)-1,3-dihydroindol-2-one
388117-19-9P 388117-20-2P 388117-21-3P
388117-22-4P, 4-(6-\text{Aminopyridin}-3-\text{yl})-3-[(3,5-\text{dimethyl}-4-(4-
methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-1,3-dihydroindol-2-one
388117-23-5P 388117-24-6P, 3-[(3,5-Dimethyl-4-(4-
methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-4-pyridin-3-yl-1,3-
dihydroindol-2-one 388117-25-7P 388117-26-8P,
5-[3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-
yl)methylene]-2-oxo-2,3-dihydro-1H-indol-4-yl]nicotinic acid
388117-28-0P 388117-29-1P, 4-(2-Aminopyrimidin-5-yl)-3-
[(3,5-dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-
1,3-dihydroindol-2-one 388117-30-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (drug; prepn. and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones
   and their use as protein kinase inhibitors)
388116-44-7 CAPLUS
Piperazine, 1-\{[5-\{[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-
ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI)
INDEX NAME)
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RN

CN

RN 388116-47-0 CAPLUS
CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-50-5 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 388116-51-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$H$$
 O
 CH
 H
 N
 Me
 $HO_2C-CH_2-CH_2$

RN 388116-52-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-ethyl- (9CI) (CA INDEX NAME)

RN 388116-54-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} O \\ H \\ N \\ \end{array} \begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} Me \\ C \\ C \\ O \end{array}$$

RN 388116-55-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm O}$ $^{\rm H}_{
m N}$ $^{\rm Me}$ $^{\rm CH}_2-{\rm CH}_2-{\rm CO}_2{\rm H}$

RN 388116-56-1 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-57-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-pyridinyl)-

(9CI) (CA INDEX NAME)

RN 388116-60-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-61-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-64-1 CAPLUS

CN lH-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-65-2 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-2-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-66-3 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 388116-68-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)

RN 388116-73-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & O \\ \hline & H & C-OEt \\ \hline & HO_2C-CH_2-CH_2 & Me \\ \hline \end{array}$$

RN 388116-74-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

RN 388116-76-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 388116-80-1 CAPLUS

CN Piperidine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-81-2 CAPLUS

CN Morpholine, 4-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-86-7 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 388116-87-8 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 388116-88-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} O \\ CH \\ \end{array} \begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} M \\ G \\ \end{array}$$

RN 388116-89-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-ethyl- (9CI) (CA INDEX NAME)

RN 388116-90-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & H & O & H & Me \\ \hline & HO_2C-CH_2-CH_2 & C-OEt & H & O \\ \hline & H & O & O & H \\ \hline & O & O & O & O \\ \end{array}$$

RN 388116-91-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & Me \\ \hline & CH_2-CH_2-CO_2H \\ \hline & N & H \\ \end{array}$$

RN 388116-92-5 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-93-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-piperidinyl)-(9CI) (CA INDEX NAME)

RN 388116-96-9 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-97-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-99-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388117-00-8 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-2-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-01-9 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-02-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)

RN 388117-05-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidiny1)-3H-indol-3-ylidene]methyl]-5-(ethoxycarbony1)-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-06-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

RN 388117-07-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-08-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 388117-10-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 388117-12-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 388117-14-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(2-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-,

ethyl ester (9CI) (CA INDEX NAME)

RN 388117-16-6 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(2-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-17-7 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(5-pyrimidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl-(9CI) (CA INDEX NAME)

RN 388117-18-8 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(2-thiazolyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-19-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(5-pyrimidinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-20-2 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(2-thiazolyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-21-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[4-(6-amino-3-pyridinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-22-4 CAPLUS

CN Piperazine, 1-[[5-[[4-(6-amino-3-pyridinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-23-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-,

ethyl ester (9CI) (CA INDEX NAME)

RN 388117-24-6 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-25-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[3-[[4-(ethoxycarbonyl)-5-methyl-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-4-yl]- (9CI) (CA INDEX NAME)

RN 388117-26-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[3-[[3,5-dimethyl-4-[(4-methyl-1-piperazinyl)carbonyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-4-yl]- (9CI) (CA INDEX NAME)

RN 388117-28-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[4-(2-amino-5-pyrimidinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388117-29-1 CAPLUS

CN Piperazine, 1-[[5-[[4-(2-amino-5-pyrimidinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-30-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

IT **388116-49-2P**, 3-(3,5-Dimethyl-1H-pyrrol-2-ylmethylene)-4-(pyridin-4-yl)-1,3-dihydroindol-2-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones and their use as **protein kinase** inhibitors)

RN 388116-49-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Journal

LANGUAGE: English AΒ

Angiogenesis is crit. for tumor development, growth and metastasis. vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF) and their tyrosine kinase receptors are major regulators of angiogenesis. Radiation induces the prodn. of VEGF, FGF and PDGF in many tumor cells. We hypothesized that inhibition of the function of these growth factors could inhibit tumor angiogenesis and thereby enhance the efficacy of radiation therapy. test this hypothesis, we used the small mol. inhibitors SU5416 (an inhibitor for Vegf receptor) and SU6668 (an inhibitor for Vegf, Fgf and Pdgf receptors) alone and in combination with fractionated irradn. to treat C3H mice bearing SCC VII carcinomas. The SCC VII tumors express Vegf, Fgf2 (also known as bFGF), Pdgf and their assocd. receptors. Animals were given either SU5416 or SU6668 daily before or after irradn. (2 Gy per fraction per day for 5 days). The results from these expts. demonstrate that administration of either SU5416 or SU6668 without radiation delayed tumor growth. Administration of SU5416 at a dose of 25 mg/kg per day (the max. tolerated ED) inhibited tumor growth by 17.9% on day 7 (P < 0.05 compared to untreated control mice) and produced an av. tumor growth delay time of 0.5-2.0 days. When combined with fractionated irradn., administration of SU5416 increased the inhibition of tumor growth to 50-53% on day 7 and the tumor growth delay time to 5.7-6.5 days (P < 0.001 compared with SU5416 alone; P 0.05 compared with radiation alone). SU6668 alone inhibited tumor growth in a dose-dependent manner. Administration of SU6668 at a dose of 75 mg/kg per day (a suboptimal dose) inhibited tumor growth by 36% on day 7 and produced an av. tumor growth delay time of 3.3 .+-. 1.4 days. The combination of SU6668 with fractionated radiation increased inhibition of tumor growth to 66-70% and the tumor growth delay time from 3.3 days to 11.9 days (P .ltoreq. 0.001 compared with either radiation alone or SU6668 alone). Administration of these agents before or after irradn. produced similar results (P = 0.40for SU5416; P = 0.98 for SU6668). SU5416 or SU6668 alone or in combination with radiation was very well tolerated with little or no toxicity. These results suggest that inhibition of Vegf, Fgf and Pdgf receptor function by SU5416 and SU6668 can enhance the efficacy of irradn. The targeting of multiple tyrosine kinase receptors by SU6668 is more effective than inhibition of the Vegf receptor alone by SU5416 for the enhancement of tumor cell killing by fractionated irradn.

ΙT 204005-46-9, SU5416

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiangiogenic agents SU5416 and SU6668 increase antitumor effects of fractionated irradn.)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (CA INDEX NAME)

REFERENCE COUNT:

41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 5 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:904107 CAPLUS

DOCUMENT NUMBER:

TITLE:

136:37505

Preparation of 3-(2-indolylmethylene)-2-indolinones as

protein_kinase/phosphatase inhibitors for treatment of proliferative diseases Tang, Peng Cho; Harris, G. Davis; Li, Xiaoyuan

INVENTOR(S): PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 199 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

•	PATENT NO. KII			ND :	DATE		APPLICATION NO.						DATE					
	WO-2001-094312 A					20011213				WO 2001-US17961					20010604			
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	
		RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	
		UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	MT			
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
PRIORITY APPLN. INFO.:					US 2000-209162P P 20000602													
OTHER SOURCE(S):				MARPAT 136:37505														

Title compds. I [wherein R4-R6 and R8-R10 = H; R1, R2, and R3 = $\frac{1}{2}$ AΒ independently H, halo, carboxylic acid, trihalomethyl, or (un)substituted ester, amide, alkyl, alkoxy, or (hetero)aryl; R7 = (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salt thereof] were prepd. as modulators of the activity of protein kinases (PKs) and phosphatases. For example, 5-bromo-2-oxindole was coupled with 5-(3-diethylaminopropyl)-1H-indole-2-carbaldehyde (prepn. given) in the presence of piperidine in EtOH to afford II, which inhibited GST-FLK-1, EGF receptor kinase, and PDGF with IC50 values of 0.03 .mu.M, 2.87 .mu.M, and 0.38 .mu.M, resp. I are useful in treating disorders related to abnormal PK activity, such as blood vessel proliferative disorders, mesangial cell proliferative disorders, fibrotic disorders, cancer, diabetes, autoimmune disorders, hyperproliferation disorders, restenosis, fibrosis, psoriasis, von Heppel-Lindau disease, osteoarthritis, rheumatoid arthritis, angiogenesis, inflammatory disorders, immunol. disorders, and cardiovascular disorders (no data). Combinatorial libraries comprising at least five indolinone compds., formed by reacting oxindoles with aldehydes, are also claimed.

II

IT 258830-88-5P

RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (indolylmethylene)indolinones as **protein kinase**/phosphatase inhibitors for treatment of proliferative diseases)

RN 258830-88-5 CAPLUS CN 1H-Indole-5-sulfona

1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N,N-dimethyl-2-oxo-(9CI) (CA INDEX NAME)

IT 258830-79-4P 380241-29-2P 380241-30-5P

380241-31-6P 380241-33-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use)

; BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)indolinones as protein

kinase/phosphatase inhibitors for treatment of proliferative

diseases)

RN 258830-79-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ \hline O & & H & O \\ \hline MeNH-S & & CH & M \\ \hline O & & H & \\ \hline \end{array}$$

RN 380241-29-2 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O \\ \hline & N \\ Br & \\ \end{array}$$

RN 380241-30-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)

RN 380241-31-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl-(9CI) (CA INDEX NAME)

RN 380241-33-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

IT 258830-66-9P 380242-44-4P 380242-45-5P 380242-46-6P 380242-47-7P 380242-48-8P 380242-49-9P 380242-50-2P 380242-51-3P 380242-52-4P 380242-53-5P 380242-54-6P 380242-55-7P 380242-56-8P 380242-57-9P 380242-58-0P 380242-59-1P 380242-60-4P 380242-61-5P 380242-62-6P 380242-63-7P 380242-64-8P 380242-65-9P 380242-66-0P 380242-67-1P 380242-68-2P 380242-69-3P 380242-70-6P 380242-71-7P 380242-72-8P 380242-73-9P 380363-16-6P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses) (prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

RN 258830-66-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ H_2N-S & \\ & & \\ O & \\ \end{array}$$

RN 380242-44-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & (CH_2)_3 - NEt_2 \\ \hline Me_2N - S & . & H \\ \hline \\ O & . & H \end{array}$$

RN 380242-45-5 CAPLUS

CN Piperazine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-4-methyl-(9CI) (CA INDEX NAME)

RN 380242-46-6 CAPLUS

CN Pyrrolidine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

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RN 380242-47-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyethyl)-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & N & O \\
 & MeO-CH_2-CH_2-NH-S \\
 & O & H
\end{array}$$
(CH₂) 3-NEt₂

RN 380242-48-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)

RN 380242-49-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyphenyl)-2-oxo- (9CI) (CA INDEX NAME)

RN 380242-50-2 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-51-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-N-[(4-fluorophenyl)methyl]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-52-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & H_2N-S & H \\
 & O & H
\end{array}$$

$$\begin{array}{c|c}
 & CH & N & H \\
 & N & H & H
\end{array}$$

$$\begin{array}{c|c}
 & CH_2)_3-NEt_2 \\
 & N & H
\end{array}$$

RN 380242-53-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-54-6 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 380242-55-7 CAPLUS

CN Pyrrolidine, 1-[[2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 380242-56-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-methoxyethyl)-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{MeO-CH}_2\text{-CH}_2\text{-NH-S} & & \\ & & \\ & & \\ & & \\ \end{array}$$

RN 380242-57-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-methoxyphenyl)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-58-0 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} C1 & & H & O \\ NH - S & & CH & N \\ O & & & H \end{array}$$

RN 380242-59-1 CAPLUS

CN 1H-Indole-5-sulfonamide, N-[(4-fluorophenyl)methyl]-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} F & & & & & & \\ \hline \\ CH_2-NH-S & & & & \\ \hline \\ O & & & \\ \end{array}$$

RN 380242-60-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(1-methylethyl)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-61-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 380242-62-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 380242-63-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 380242-64-8 CAPLUS

CN 1H-Indole-4-carboxylic acid, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ CH \\ CO_2H \end{array}$$

RN 380242-65-9 CAPLUS

CN 2H-Indol-2-one, 6-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 380242-66-0 CAPLUS

CN 1H-Indole-4-carboxamide, N-(3-chloro-4-methoxyphenyl)-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI)(CA INDEX NAME)

RN 380242-67-1 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380242-68-2 CAPLUS

CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 380242-69-3 CAPLUS

CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

N— (CH₂) 3

$$\begin{array}{c} H \\ N \end{array}$$
 $\begin{array}{c} C \\ N \end{array}$
 $\begin{array}{c} C \\ N \end{array}$
 $\begin{array}{c} C \\ N \end{array}$

RN 380242-70-6 CAPLUS

CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$(CH_2)_3$$

$$(CH_2)_3$$

$$(CH_2)_3$$

$$(CH_2)_3$$

$$(CH_2)_3$$

RN 380242-71-7 CAPLUS

CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 380242-72-8 CAPLUS

CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$(CH_2)_3$$

$$0$$

$$N$$

$$N$$

$$O$$

$$M$$

$$O$$

$$M$$

$$O$$

$$M$$

RN 380242-73-9 CAPLUS

CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$(CH_2)_3$$

$$0$$

$$N$$

$$0$$

$$N$$

$$0$$

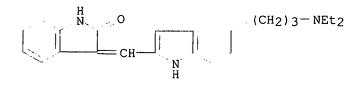
$$CO_2H$$

RN 380363-16-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(pyridinyl)- (9CI) (CA INDEX NAME)

yl)methylene]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)

```
IT
     380241-13-4P 380241-14-5P 380241-15-6P
     380241-16-7P 380241-17-8P 380241-18-9P
     380241-19-0P 380241-20-3P 380241-21-4P
     380241-22-5P 380241-23-6P 380241-24-7P
     380241-25-8P 380241-26-9P 380241-27-0P
     380241-28-1P 380241-32-7P 380241-34-9P
     380241-35-0P 380241-36-1P 380241-37-2P
     380241-38-3P 380241-39-4P 380241-40-7P
     380241-41-8P 380241-42-9P 380241-43-0P
     380241-44-1P 380241-45-2P 380241-46-3P
     380241-47-4P 380241-48-5P 380241-49-6P
     380241-50-9P 380241-51-0P 380241-53-2P
     380241-54-3P 380241-56-5P 380241-59-8P
     380241-61-2P 380241-65-6P 380241-68-9P
     380241-71-4P 380241-74-7P 380241-78-1P
     380241-82-7P 380241-84-9P 380241-86-1P
     380241-88-3P 380241-90-7P 380241-91-8P
     380241-92-9P 380241-93-0P 380241-94-1P
     380241-95-2P 380241-96-3P 380241-97-4P
     380241-98-5P 380241-99-6P 380242-00-2P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
     THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of (indolylmethylene)indolinones as protein
        kinase/phosphatase inhibitors for treatment of proliferative
        diseases)
RN
     380241-13-4 CAPLUS
CN
     2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-
     1,3-dihydro- (9CI) (CA INDEX NAME)
```



RN 380241-14-5 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow CH$$
 $(CH_2)_3 - NEt_2$

RN 380241-15-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl-(9CI) (CA INDEX NAME)

RN 380241-16-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

Ph
$$CH \longrightarrow N$$
 $CH \longrightarrow N$ H $CH \longrightarrow N$ H

RN 380241-17-8 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

RN 380241-18-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-19-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H \\ & N \\ \hline \\ O \end{array} \qquad \begin{array}{c} H \\ & N \\ \hline \\ O \end{array} \qquad \begin{array}{c} H \\ & N \\ \end{array} \qquad \begin{array}{c} CH \\ & N \\ \end{array} \qquad \begin{array}{c} H \\ & N \\ \end{array} \qquad \begin{array}{c} CH \\ & N \\ \end{array} \qquad \begin{array}{c} H \\ \\ \end{array}$$

RN 380241-20-3 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$N$$
 CH_2 CH_2 O O N H O N H

RN 380241-21-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-phenyl- (9CI) (CA INDEX NAME)

RN 380241-22-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 380241-23-6 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{H} \\ \text{N} \\ \text{O} \\ \text{CH} \\ \text{H} \end{array} \\ \begin{array}{c} \text{O-CH}_2\text{-CH}_2\text{-NMe}_2 \\ \\ \text{N} \\ \text{H} \end{array}$$

RN 380241-24-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl-(9CI) (CA INDEX NAME)

RN 380241-25-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$N - CH_2 - CH_2 - O$$
 $N - CH_2 - CH_2 - O$
 $N - CH_2 - CH_2 - O$
 $N - CH_2 - CH_2 - O$
 $N - CH_2 - CH_2 - O$

RN 380241-26-9 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-27-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-28-1 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-

1,3-dihydro- (9CI) (CA INDEX NAME)

RN 380241-32-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-34-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$CH_2-CH_2-O$$
 H
 CH_2-CH_2-O
 H
 CH_2-CH_2-O
 H
 CH_2-CH_2-O
 H

RN 380241-35-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & N - CH_2 - CH_2 - O & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 380241-36-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & CH_2-CH_2-OH \\ \hline \\ N-CH_2-CH_2-O \\ \hline \\ N \\ H \end{array}$$

RN 380241-37-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-pyridinyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-38-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-39-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-40-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$N-CH_2-CH_2-O$$
 $N-CH_2-CH_2-O$
 $N-CH_2-CH_2-$

RN 380241-41-8 CAPLUS

CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-42-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-43-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-44-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-5-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \hline \\ O & & \\ \hline \end{array} \qquad \begin{array}{c} H \\ N \\ \hline \\ CH \\ \hline \end{array} \qquad \begin{array}{c} Ph \\ \\ O \\ H \end{array}$$

RN 380241-45-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-46-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-(3-pyridinyl)- (9CI) (CA INDEX NAME)

RN 380241-47-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \text{N} \\ \text{CH} \\ \text{H} \end{array} \\ \begin{array}{c} \text{O} \\ \text{CH}_2 \\ \text{CH}_2 \\ \end{array}$$

RN 380241-48-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ O \\ CH \\ \end{array}$$

RN 380241-49-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-50-9 CAPLUS

CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

F
$$O-CH_2-CH_2-N$$
 $O-CH_2-CH_2-N$

RN 380241-51-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ H \\ N \\ \end{array}$$

$$\begin{array}{c} O \\ S \\ \end{array}$$

$$\begin{array}{c} O \\ N \\ \end{array}$$

$$\begin{array}{c} O \\ S \\ \end{array}$$

$$\begin{array}{c} O \\ N \\ \end{array}$$

RN 380241-53-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ H \\ N \\ CH_2 \\ CH_2 \\ O \end{array}$$

RN 380241-54-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-56-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-59-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-61-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-65-6 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-3-pyridinyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-68-9 CAPLUS

CN 1H-Indole, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro-(9CI) (CA INDEX NAME)

$$O = S$$

$$O = S$$

$$O = H$$

$$O = CH_2 - CH_2 - N$$

RN 380241-71-4 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$N-CH_2-CH_2-O$$
 $N-CH_2-CH_2-O$
 $N-CH_2-CH_2-$

PAGE 1-B

__Cl

RN 380241-74-7 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-78-1 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} & & & \\ & & \\ N - CH_2 - CH_2 - O \end{array}$$

Searched by Barb O'Bryen, STIC 308-4291

PAGE 1-B

__ C1

RN 380241-82-7 CAPLUS

CN Quinoline, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro-(9CI) (CA INDEX NAME)

$$O = S$$

$$O = S$$

$$CH = M$$

$$H$$

$$O = CH_2 - CH_2 - M$$

RN 380241-84-9 CAPLUS

CN Isoquinoline, 2-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & N \\
 & S \\
 & O \\
 & O \\
 & O \\
 & CH \\
 & H \\
 & O \\
 & O \\
 & CH_2 - CH_2 - N \\
 & O \\$$

RN 380241-86-1 CAPLUS

CN 1H-Indole, 5-bromo-1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Br
$$O = CH_2 - CH_2 - N$$
 $O = CH_2 - CH_2 - N$

RN 380241-88-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & \\ N - CH_2 - CH_2 - O \end{array}$$

RN 380241-90-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

RN 380241-91-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 380241-92-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-phenyl- (9CI) (CA INDEX NAME)

RN 380241-93-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ N & & \\$$

RN 380241-94-1 CAPLUS

CN 1H-Indole, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & O & CH_2 - CH_2 - N \\
 & O & H
\end{array}$$

RN 380241-95-2 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} & & & \\ &$$

PAGE 1-B

$$-N$$

RN 380241-96-3 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me O} & \text{H} & \text{O} \\ \text{N-S} & \text{CH-N} & \text{H} \\ \text{O} & \text{H} & \text{O} \\ \end{array}$$

RN 380241-97-4 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} C1 & O & H \\ \hline \\ NH - S & CH \\ \hline \\ F & O \end{array}$$

PAGE 1-B

$$-N$$

RN 380241-98-5 CAPLUS

CN Quinoline, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro-(9CI) (CA INDEX NAME)

$$O = S$$

$$CH = N$$

$$N$$

$$H$$

$$O = CH_2 - CH_2 - N$$

RN 380241-99-6 CAPLUS

CN Isoquinoline, 2-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380242-00-2 CAPLUS

CN 1H-Indole, 5-bromo-1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Br
$$O = S$$
 $CH = N$ $O = CH_2 - CH_2 - N$ $O = CH_2 - CH_2 - N$

L65 ANSWER 6 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:868450 CAPLUS

DOCUMENT NUMBER:

136:5903

TITLE:

Preparation of 1-(pyrrolidin-1-ylmethyl)-3-(pyrrol-2-

ylmethylidene) -2-indolinones as protein

kinase activity modulators.

INVENTOR(S):

Moon, Malcolm Wilson; Morozowich, Walter; Gao, Ping

Pharmacia + Upjohn Company, USA

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 83 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

3

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	PATENT NO.			KIND DATE					PPLI	CATI	ON NC	Э.	DATE				
WO_2001	A220011129					M-	0 20	01-U	S167	 56	20010524						
W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ÃŻ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	
	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	ΝZ,	PL,	PT,	
	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	
	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM			
RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZW,	ΑT,	ΒE,	CH,	CY,	
	DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
US 2002	US 2002032204 A1					0314		U	S 20	01-8	6380	20010524					
US 2002	US 2002035140 A1					0321		U	S 20	01-8	6390	5	20010524				
US 2002	US 2002037878 A1					0328	US 2001-863819 20010524										
PRIORITY APE	PRIORITY APPLN. INFO.:								US 2000-207000P P 20000524								
								US 2	000-	2250	45P	Р	2000	0811			

OTHER SOURCE(S):

MARPAT 136:5903

Ι

GI

AB Title compds. [I; R3-R6 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, SH, alkylthio, arylthio, etc.; .gtoreq.2 of R3-R6 = H; R7 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, aryloxy, etc.; R8-R10 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, aryloxy, SH, alkylthio, arylthio, etc.], were prepd. Thus, pyrrolidine was added to a mixt. of aq. H2CO and 3-(3,5-dimethyl-1H-pyrrol-2-ylmethylidene)-1,3-dihydroindol-2-one in MeOH; after 15 min. the mixt. was cooled to 0.degree. and filtered to give (3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylidene]-1-(1-pyrrolidinylmethyl)-1,3-dihydro-2H-indol-2-one. The latter prodrug had a half life of 7.3 min. in dogs.

IT 375387-20-5P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyrrolidinylmethylpyrrolylmethylideneindolinones as protein kinase activity modulators)

RN 375387-20-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(1-pyrrolidinylmethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 204005-46-9

CN

RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of pyrrolidinylmethylpyrrolylmethylideneindolinones as
 protein kinase activity modulators)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 7 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:868415 CAPLUS

DOCUMENT NUMBER: 136:697

TITLE: Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-

indolinone derivatives

INVENTOR(S): Moon, Malcolm Wilson; Morozowich, Walter; Gao, Ping;

Page 78

Tang, Peng Cho

PATENT ASSIGNEE(S): Sugen, Inc., USA; Pharmacia + Upjohn Company

SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.				KIND DATE				APPLICATION NO. DATE										
WO	2001090068			A2 20011129				WO 2001-US16757 20010524										
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	
		RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	
		UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM			
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	ΙT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
US	US 2002032204					A1 20020314					US 2001-863804 20010524							
US	US 2002035140				A1 20020321				US 2001-863905 20010524									
US	2002	0378	78	Α	1	2002	0328		U.	S 20	01-8	6381	9	2001	0524			
PRIORITY APPLN. INFO.: US 2000-207000P P 20000524																		
								1	US 2	000-	2250	45P	Ρ	2000	0811			

OTHER SOURCE(S): MARPAT 136:697

AB The present invention is directed to Mannich base prodrugs of certain 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs. that modulate the activity of protein kinases ("PKs"). Pharmaceutical compns. comprising these compds., methods of treating diseases related to abnormal

comprising these compds., methods of treating diseases related to abnormal PK activity utilizing pharmaceutical compns. comprising these compds. and methods of prepg. them are also disclosed.

IT 375387-20-5P 375798-46-2P

RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone

derivs.)

RN 375387-20-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(1-pyrrolidinylmethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-46-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1[(4-methyl-1-piperazinyl)methyl]-, dihydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●2 HCl

IT 326914-13-0P 375798-54-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 326914-13-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-54-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(hydroxymethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 375798-45-1P 375798-47-3P 375798-48-4P

375798-49-5P 375798-50-8P 375798-51-9P

375798-52-0P 375798-53-1P 375798-55-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375798-45-1 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-47-3 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-hydroxy-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-48-4 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-methyl-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-49-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[[2-(methoxymethyl)-1-pyrrolidinyl]methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-50-8 CAPLUS

CN L-Proline, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol+2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 375798-51-9 CAPLUS

CN 2H-Indol-2-one, 1-[(3,5-dimethyl-1-piperazinyl)methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-52-0 CAPLUS

CN 2H-Indol-2-one, 1-[[bis(2-methoxyethyl)amino]methyl]-3-[(3,5-dimethyl-1H-

pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-53-1 CAPLUS

CN Pyridinium, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● C1-

RN 375798-55-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & NEt \\ \hline Z & Me & OH \\ \hline \end{array}$$

L65 ANSWER 8 OF 70

CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:617993 CAPLUS

DOCUMENT NUMBER:

135:195497

TITLE:

ole substituted 2-indolinone

protein kinase inhibitors for

treatment of cancer...

INVENTOR(S): Tang, Peng Cho; Miller, Todd; Li, Xiaoyuan; Sun, Li;

Wei, Chung Chen; Shirazian, Shahrzad; Liang, Congxin;

Vojkovsky, Tomas; Nematalla, Asaad S.

PATENT ASSIGNEE(S):

SOURCE:

Sugen, Inc., USA

PCT Int. Appl., 225 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.			KIND DATE		DATE			A.	PPLI	٥.	DATE								
WO WO	70 2001060814 A2					2001. 2002.	08 <u>23</u> 0124	Mar of	WO 2001-US4813						20010215				
	W:					AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
		CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,		
		HU,	ID,	TL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,		
		LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,		
														UG,					
						AZ,													
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪG,	ZW,	AT,	BE,	CH,	CY,		
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,		
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG	•	•		
PRIORITY APPLN. INFO.:								1	US 20	000-	1827	10P	P	20000	0215				
								1	US 20	000-	2164	22P	P	20000	0706				
								1	US 20	000-	2435	32P	P	2000	1027		,		

OTHER SOURCE(S):

MARPAT 135:195497

GΙ

$$R^{2}$$
 R^{3}
 R^{4}
 R^{7}
 R^{6}
 R^{7}
 R^{6}
 R^{7}
 R^{6}
 R^{7}
 R^{6}
 R^{7}
 R^{6}

ΑB The title compds. (I) [wherein R1 = H, halo, (cyclo)alkyl, (hetero)aryl, heteroalicyclic, OH, alkoxy, acyl, (un) substituted amino or carbamoyl, etc.; R2 = H, halo, alkyl, trihalomethyl, OH, alkoxy, CN, (hetero)aryl,

II

Ι

(un) substituted amino, acyl (amino), or sulfamoyl, etc.; R3 = H, halo, alkyl, trihalomethyl, OH, alkoxy, (hetero)aryl, (un) substituted acyl, (acyl)amino, sulfamoyl, or alkylsulfonyl, etc.; R4 = H, halo, alkyl, OH, alkoxy, or (un) substituted amino; R5 and R6 = independently H, alkyl, or acyl; R7 = H, alkyl, (hetero)aryl, or acyl; and their pharmaceutically acceptable saltsl were prepd. as protein kinase modulators for the treatment of cellular disorders such as cancer. For example, 5-fluoro-1,3-dihydroindol-2-one was condensed with 5-formyl-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide to give II (55%). II exhibited comparable activity against Flk-1 and PDGFR.beta. and inhibited PDGF-dependent receptor phosphorylation in cells with an IC50 value of approx. 0.03 .mu.M. In efficacy expts. against various cancers in mice, II was well tolerated at 80 mg/kg/day, even when dosed continuously for more than 100 days.

IT 356068-93-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of

dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

RN 356068-93-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & \text{Me} & \text{CO}_2H \\ \hline Z & & \\ H & & \\ \end{array}$$

IT 326914-13-0P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of pyrrole substituted 2-indolinone protein

kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

RN 326914-13-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & NEt_2 \\ \hline Z & Me \\ \hline M & Me \\ \end{array}$$

IT 280748-39-2P 280748-40-5P 326914-09-4P

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326914-10-7P 326914-17-4P 326914-19-6P
342641-15-0P 342641-16-1P 342641-17-2P
342641-18-3P 342641-19-4P 342641-20-7P
342641-21-8P 342641-22-9P 342641-23-0P
342641-24-1P 342641-25-2P 342641-26-3P
342641-27-4P 342641-28-5P 342641-29-6P
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342641-46-7P 342641-47-8P 342641-48-9P
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342641-62-7P 342641-63-8P 342641-64-9P
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356069-69-7P 356069-70-0P 356069-71-1P
356069-72-2P 356069-73-3P 356069-74-4P
356069-75-5P 356069-76-6P 356069-77-7P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
```

(prepn. of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

RN 280748-39-2 CAPLUS

CN

1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 280748-40-5 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 326914-09-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 326914-10-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 326914-17-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(dimethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me & O \\ \hline N & N & Me \\ \hline Z & N & Me \\ \hline N & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 326914-19-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 342641-15-0 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-1-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 342641-16-1 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Jones

RN 342641-17-2 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 342641-18-3 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-19-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-4-methyl- (9CI) (CA INDEX NAME)

Br
$$C-NH-(CH_2)_3-NEt_2$$

RN 342641-20-7 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow CH \longrightarrow CH_2 - CH_2 - NEt_2$$

RN 342641-21-8 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

Ph
$$\stackrel{H}{\sim}$$
 O $\stackrel{O}{\sim}$ C $\stackrel{H}{\sim}$ C $\stackrel{C}{\sim}$ NH $\stackrel{C}{\sim}$ CH $\stackrel{C}{\sim}$ NEt 2

RN 342641-22-9 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-N-methyl- (9CI) (CA_INDEX NAME)

RN 342641-23-0 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-N-methyl- (9CI) (CA INDEX NAME)

RN 342641-24-1 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

RN 342641-25-2 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-3-methyl- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow CH \longrightarrow CH \longrightarrow CH$$
 $C-NH-(CH2)3-NEt2$

RN 342641-26-3 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-3-methyl- (9CI) (CA INDEX NAME)

RN 342641-27-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl- (9CI) (CA INDEX NAME)

RN 342641-28-5 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl- (9CI) (CA INDEX NAME)

RN 342641-29-6 CAPLUS

CN 2H-Isoindole-1-carboxamide, 3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 342641-30-9 CAPLUS

CN 2H-Isoindole-1-carboxamide, 3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 342641-31-0 CAPLUS

CN 2H-Isoindole-1-carboxamide, 3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-32-1 CAPLUS

CN 2H-Isoindole-1-carboxamide, N-[2-(diethylamino)ethyl]-3-[[1,2-dihydro-2-oxo-6-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 342641-33-2 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-3-methyl- (9CI) (CA INDEX NAME)

Br.
$$CH \longrightarrow Me$$
 $CH \longrightarrow Me$ $CH \longrightarrow Me$ $CH \longrightarrow Me$

RN 342641-35-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ Br & \\ & & \\$$

RN 342641-36-5 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-37-6 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

- RN 342641-38-7 CAPLUS
- CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

- RN 342641-39-8 CAPLUS
- CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\stackrel{N}{\stackrel{}}}$$
 $\stackrel{O}{\stackrel{}}$ $\stackrel{H}{\stackrel{}}$ $\stackrel{O}{\stackrel{}}$ $\stackrel{C}{\stackrel{}}$ $\stackrel{N}{\stackrel{}}$ $\stackrel{C}{\stackrel{}}$ $\stackrel{N}{\stackrel{}}$ $\stackrel{C}{\stackrel{}}$ $\stackrel{N}{\stackrel{}}$ $\stackrel{C}{\stackrel{}}$ $\stackrel{N}{\stackrel{}}$ $\stackrel{N}{\stackrel{N}{\stackrel{}}}$ $\stackrel{N}{\stackrel{}}$ $\stackrel{N}{\stackrel{N}}$ $\stackrel{N}{\stackrel{N}{\stackrel{}}$ $\stackrel{N}{\stackrel{N}}$ \stackrel{N} \stackrel{N}

- RN 342641-40-1 CAPLUS
- CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-41-2 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-benzoyl-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-42-3 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-3-methyl- (9CI) (CA INDEX NAME)

RN 342641-43-4 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-44-5 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow CH \longrightarrow CH \longrightarrow CH \longrightarrow CH_2)_3 \longrightarrow N$$

RN 342641-45-6 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-(3-hydroxypropyl)-3-methyl- (9CI) (CA INDEX NAME)

RN 342641-46-7 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-47-8 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Br
$$\stackrel{H}{N}$$
 $\stackrel{O}{\longrightarrow}$ $\stackrel{H}{\longrightarrow}$ $\stackrel{O}{\longrightarrow}$ $\stackrel{H}{\longrightarrow}$ $\stackrel{O}{\longrightarrow}$ $\stackrel{C}{\longrightarrow}$ \stackrel

RN 342641-48-9 CAPLUS

CN 1H-Pyrrole-2-carboxamide, 4-acetyl-5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(4-hydroxyphenyl)ethyl]-3-methyl- (9CI) (CA INDEX NAME)

Br
$$\stackrel{H}{\sim}$$
 $\stackrel{O}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{O}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{O}{\sim}$ \stackrel

RN 342641-49-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-2-(1-methylethyl)-4-phenyl-(9CI) (CA INDEX NAME)

RN 342641-50-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(1-methylethyl)-4-phenyl-N-[3-(1-pyrrolidinyl)propyl]-(9CI) (CA INDEX NAME)

RN 342641-51-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-2-(1-methylethyl)-4-phenyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ Br & & \\ & &$$

RN 342641-52-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(1-methylethyl)-N-[3-(4-methyl-1-piperazinyl)propyl]-4-phenyl- (9CI) (CA INDEX NAME)

RN 342641-54-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-4-phenyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-55-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-phenyl-N-[2-(1-pyrrolidinyl)ethyl]-(9CI) (CA INDEX NAME)

RN 342641-56-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow Me$$
 $CH \longrightarrow Me$
 $C-NH-CH_2-CH_2-NMe_2$

RN 342641-57-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(dimethylamino)ethyl]-2-methyl-4-phenyl-(9CI) (CA INDEX NAME)

RN 342641-58-1 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 342641-59-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-2-methyl-4-phenyl- (9CI) (CA INDEX NAME)

09/716332

RN 342641-60-5 CAPLUS

1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-61-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-62-7 CAPLUS

1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

C1

$$H$$
 CH
 H
 N
 Me
 $C-NH-CH_2-CH_2-NMe_2$
 H
 O

RN342641-63-8 CAPLUS

1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ & H & Me \\ & CH & Me \\ & Me & C-NH-CH_2-CH_2-NEt_2 \\ & \parallel & O \end{array}$$

RN 342641-64-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-65-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1H-imidazol-1-yl)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-66-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

- RN 342641-67-2 CAPLUS
- CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

- RN 342641-68-3 CAPLUS
- CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Ph
$$CH \longrightarrow Me$$
 $C-NH-CH_2-CH_2-NEt_2$
 $C-NH-CH_2-CH_2-NEt_2$

- RN 342641-69-4 CAPLUS
- CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-70-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-N-[3-(1H-imidazol-1-yl)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-71-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Ph
$$\stackrel{H}{\stackrel{N}{\stackrel{}}}$$
 $\stackrel{O}{\stackrel{CH}{\stackrel{}}}$ $\stackrel{H}{\stackrel{N}{\stackrel{}}}$ $\stackrel{Me}{\stackrel{C-NH-CH_2-CH_2-NEt_2}{\stackrel{}}}$

RN 342641-72-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-

ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-73-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-N-[3-(1H-imidazol-1-yl)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-74-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[6-(3,5-dichlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

C1

$$H$$
 CH
 Me
 $C-NH-CH_2-CH_2-NEt_2$
 O

RN 342641-75-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-6-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-76-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-6-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-77-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-6-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-N-[3-(dimethylamino)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN. 342641-78-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-N-[3-(dimethylamino)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-79-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 342641-80-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)propyl]-5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Ph
$$\stackrel{H}{N}$$
 $\stackrel{O}{CH}$ $\stackrel{H}{N}$ $\stackrel{Me}{Me}$ $\stackrel{C-NH-(CH_2)}{O}$ $\stackrel{NEt_2}{O}$

RN 342641-81-0 CAPLUS

CN 1H-Indole-4-carboxamide, N-(3-chloro-4-methoxyphenyl)-3-[[4-[[[3-(diethylamino)propyl]amino]carbonyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 342641-82-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Br
$$CH \longrightarrow H$$
 N Me $C-NH-(CH2)3-NEt2$

RN 342641-83-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-2,4-bis(1-methylethyl)- (9CI) (CA INDEX NAME)

Br
$$CH$$
 CH
 CH
 $C-NH-CH_2-CH_2-NEt_2$
 C
 C

RN 342641-84-3 CAPLUS

CN lH-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(diethylamino)propyl]-2,4-bis(1-methylethyl)- (9CI) (CA INDEX NAME)

RN 342641-85-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-bis(1-methylethyl)-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 342641-87-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 342641-88-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[6-(4-butylphenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-89-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-[2-methoxy-5-(1-methylethyl)phenyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-91-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[6-(4-ethylphenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-92-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[6-(2,4-dimethoxyphenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-93-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-6-[3-(1-methylethyl)phenyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-(9CI) (CA INDEX NAME)

RN 342641-94-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & Me & C-NH-CH_2-CH_2-NEt_2 \\ & || & O & \\ & & O & \\ \end{array}$$

RN 342641-95-6 CAPLUS

CN 1H-Indole-6-carboxylic acid, 3-[[4-[[[2-(diethylamino)ethyl]amino]carbonyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 342641-96-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[5-[(dimethylamino)sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-(9CI) (CA INDEX NAME)

RN 342641-97-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[5-[[(3-chlorophenyl)amino]sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-98-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-5-[(3-pyridinylamino)sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342641-99-0 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

HO-CH₂-CH₂

$$\begin{array}{c} H \\ N \\ CH \\ \end{array}$$

$$\begin{array}{c} H \\ N \\ Me \\ \end{array}$$

$$\begin{array}{c} Me \\ C \\ \end{array}$$

$$\begin{array}{c} N \\ N \\ \end{array}$$

$$\begin{array}{c} Me \\ \end{array}$$

$$\begin{array}{c} N \\ N \\ \end{array}$$

$$\begin{array}{c} N \\ Me \\ \end{array}$$

RN 342642-00-6 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-5-[(phenylamino)sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 342642-01-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[5-[(dimethylamino)sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 342642-02-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[5-[[(3-chlorophenyl)amino]sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

C1
$$NH-S$$
 $CH-NH-CH_2-CH_2-NEt_2$ $CH-NH-CH_2-CH_2-NEt_2$

RN 342642-03-9 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[(1,2-dihydro-2-oxo-5-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 342642-04-0 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[[1,2-dihydro-2-oxo-5-[(phenylamino)sulfonyl]-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 342642-05-1 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[4,5,6,7-tetrahydro-3-(4-morpholinylcarbonyl)-2H-isoindol-1-yl]methylene]- (9CI) (CA INDEX NAME)

RN 342642-06-2 CAPLUS

CN Pyrrolidine, 1-[[3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-2H-isoindol-1-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 342642-07-3 CAPLUS

CN 1H-Indole-6-carboxylic acid, 3-[[3-[(dimethylamino)carbonyl]-4,5,6,7-tetrahydro-2H-isoindol-1-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 342642-08-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 342642-09-5 CAPLUS

CN Glycine, N-[[5-[[1,2-dihydro-4-methyl-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 342642-10-8 CAPLUS

CN Glycine, N-[[5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-

ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 342642-11-9 CAPLUS

CN Glycine, N-[[5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 342642-12-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 342642-13-1 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 342642-14-2 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-5-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & O \\ \hline & CH & N \\ \hline & EtO-C \\ & \parallel & O \\ \end{array}$$

RN 342642-15-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 342642-16-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 342642-17-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 346405-32-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356068-82-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356068-90-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 356068-91-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & Me & C-NH-CH_2-CH_2-NEt_2 \\ & & & \\$$

RN 356068-92-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356068-94-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356068-95-6 CAPLUS

CN 1H=Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(dimethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O \\ \hline & H \\ \hline & CH \\ \hline & Me \\ \hline & C-NH-CH_2-CH_2-NMe_2 \\ \hline & O \\ \end{array}$$

RN 356068-96-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(dimethylamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & C-NH-CH_2-CH_2-NMe_2 \\ \hline & 0 & \\ \end{array}$$

RN 356068-97-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(ethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 356068-99-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethyloxidoamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & \\ \hline Z & Me \\ \hline N & Me \\ \end{array}$$

RN 356069-03-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-04-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-05-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-07-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-09-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(3,5-dimethyl-1-piperazinyl)ethyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-12-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(3,5-dimethyl-1-piperazinyl)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

RN 356069-13-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(3,5-dimethyl-1-piperazinyl)ethyl]-2,4-dimethyl-(9CI) (CA-INDEX NAME)

Double bond geometry as shown.

RN 356069-15-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(3,5-dimethyl-1-piperazinyl)ethyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

RN 356069-16-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(ethylamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & Me & C-NH-CH_2-CH_2-NHEt \\ & & & \\ & &$$

RN 356069-17-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethyloxidoamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 356069-18-6 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 356068-82-1

CMF C22 H25 C1 N4 O2

CM 2

CRN 97-67-6 CMF C4 H6 O5 CDES 1:S

Absolute stereochemistry.

RN 356069-19-7 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with N-[2-(diethylamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 342641-94-5 CMF C22 H27 F N4 O2

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & C-NH-CH_2-CH_2-NEt_2 \\ & || & O \\ \hline & O \\ \end{array}$$

CM 2

CRN 97-67-6 CMF C4 H6 O5

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CDES 1:S

Absolute stereochemistry.

RN 356069-20-0 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 356068-90-1 CMF C22 H27 C1 N4 O2

$$\begin{array}{c|c} H & O & H & Me \\ \hline CH & Me & C-NH-CH_2-CH_2-NEt_2 \\ \parallel & O & \\ \end{array}$$

CM 2

CRN 97-67-6 CMF C4 H6 O5 CDES 1:S

Absolute stereochemistry.

RN 356069-21-1 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 346405-32-1 CMF C22 H25 F N4 O2

CM 2

CRN 97-67-6 CMF C4 H6 O5 CDES 1:S

Absolute stereochemistry.

RN 356069-22-2 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with N-[2-(ethylamino)ethyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 356069-16-4 CMF C20 H23 F N4 O2

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & C-NH-CH_2-CH_2-NHEt \\ & || & O \\ \hline & O \\ \end{array}$$

CM 2

CRN 97-67-6 CMF C4 H6 O5 CDES 1:S

Absolute stereochemistry.

RN 356069-23-3 CAPLUS

CN Butanedioic acid, hydroxy-, (2S)-, compd. with N-[2-(diethyloxidoamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 356068-99-0 CMF C22 H27 F N4 O3

Double bond geometry as shown.

CM 2

CRN 97-67-6 CMF C4 H6 O5 CDES 1:S

Absolute stereochemistry.

$${\rm HO_2C} \underset{\rm OH}{\overbrace{\hspace{1.5cm}}} {\rm S} {\rm CO_2H}$$

RN 356069-24-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(acetylamino)ethyl]-5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 356069-25-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(acetylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-26-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(acetylamino)ethyl]-5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-27-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-28-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & NH \\ \hline C1 & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-29-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & NH \\ \hline Z & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-30-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & O & Me \\ \hline Z & N & Me \\ \hline N & Me \\ \end{array}$$

RN 356069-31-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & Me \\ \hline N & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-33-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(3-oxo-1-piperazinyl)ethyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 356069-32-4 CMF C22 H24 Br N5 O3

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 356069-34-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-35-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-36-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & H \\ \hline N & Me \\ \hline N & N & N \\ \hline N &$$

RN 356069-37-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(2-oxo-1-imidazolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-38-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(2-oxo-1-imidazolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-39-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(2-oxo-1-imidazolidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-40-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(2-oxo-1-imidazolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-41-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(2-oxo-1-imidazolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-42-6 CAPLUS

CN 1-Piperazineacetic acid, 4-[2-[[[5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]amino]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 356069-43-7 CAPLUS

CN 1-Piperazineacetic acid, 4-[2-[[[5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]amino]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-44-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[2-[[[5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]amino]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 356069-45-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-[(cyanomethyl)amino]ethyl]-5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-46-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(hexahydro-2-oxo-1H-azepin-1-yl)propyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-47-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(hexahydro-2-oxo-1H-azepin-1-yl)propyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & Me \\ \hline N & H \\ \hline \end{array}$$

RN 356069-48-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(hexahydro-2-oxo-1H-azepin-1-yl)propyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & Me \\ \hline \end{array}$$

RN 356069-49-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(hexahydro-2-oxo-1H-azepin-1-yl)propyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-50-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(hexahydro-2-oxo-1H-azepin-1-yl)propyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & H \\ \hline N & Me \\ \hline N & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-51-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(acetylamino)ethyl]-5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-53-9 CAPLUS
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(3-oxo-1-piperazinyl)ethyl]-,

mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 356069-52-8 CMF C22 H24 F N5 O3

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 356069-55-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(3-oxo-1-piperazinyl)ethyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 356069-54-0 CMF C22 H25 N5 O3

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 356069-57-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(3-oxo-1-piperazinyl)ethyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 356069-56-2 CMF C23 H24 N6 O3

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 356069-58-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-[(2-cyanoethyl)amino]ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N \\ \hline Z & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-59-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-[(2-cyanoethyl)amino]ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 356069-60-8 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-[(2-cyanoethyl)amino]ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-61-9 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-[(2-cyanoethyl)amino]ethyl]-5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & N & H \\ \hline Z & Me \\ \hline N & Me \\ \hline \end{array}$$

RN 356069-62-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-cyano-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-[(2-cyanoethyl)amino]ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & & & \\ &$$

RN 356069-64-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(3-oxo-1-piperazinyl)ethyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 356069-63-1 CMF C22 H24 C1 N5 O3

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 356069-65-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-66-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl}-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-67-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 356069-68-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-(4-methyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-69-7 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-70-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-71-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline N & O & Me \\ \hline Z & Me & Me \\ \hline N & Me & Me \\ \hline \end{array}$$

RN 356069-72-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-73-3 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)

RN 356069-74-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-75-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)

RN 356069-76-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 356069-77-7 CAPLUS

CN 1-Piperazineacetic acid, 4-[2-[[[5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]amino]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

IT 342641-53-6 356069-06-2 356069-08-4 356069-10-8 356069-14-2

RL: RCT (Reactant); RACT (Reactant or reagent) (reactant; prepn. of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

342641-53-6 CAPLUS CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2-(1-methylethyl)-4-phenyl- (9CI) (CA INDEX NAME)

356069-06-2 CAPLUS RN

RN

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & CH & Me \\ \hline & Me & CO_2H \\ \end{array}$$

RN 356069-08-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

356069-10-8 CAPLUS RN

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

356069-14-2 CAPLUS RN

1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-CN 3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & Me & CO_2H \\ \hline Z & Me & Me \\ \hline Me & H & Me \\ \end{array}$$

L65 ANSWER 9 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:319727 CAPLUS

DOCUMENT NUMBER:

134:316158

TITLE:

Oral formulations for camptothecin antitumor compounds

INVENTOR(S):

Muggetti, Lorena; Martini, Alessandro; Civaroli,

Paola; James, Christopher

PATENT ASSIGNEE(S):

Pharmacia + Upjohn S.p.A., Italy

SOURCE:

PCT-Int._Appl.,_30_pp/

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT 1	. OI		KI		Α	PPLI	CATI	N NC	٥.	DATE								
WO 2001	 51	71 20010503						20	1002									
			A1 20010503										20001002					
₩:	ΑE,	ΑG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,		
	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,		
	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,		
	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,		
													UG,					

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YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        GB 1999-25127
                                                         A 19991022
     The present invention relates to a semi-solid filling medium which
     comprises a camptothecin deriv.; a pharmaceutically acceptable carrier
     matrix which is a polyglycolized glyceride; and an effective
     thickening-reducing and stabilizing-promoting amt. of one or more
     pharmaceutically acceptable excipients. For example, a capsule
     formulation contg. 50 mg of CPT-11 dispersed in a mixt. of Gelucire 44/14
     and Epikuron 135F was prepd. showing good dissoln. and stability.
TT
     204005-46-9, SU 5416
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (oral formulations for camptothecin antitumor compds.)
RN
     204005-46-9 CAPLUS
     2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-
CN
           (CA INDEX NAME)
```

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 10 OF 70 CAPLUS COPYRIGHT 2002 ACS 2001:208110 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:242681

TITLE:

Formulations for parenteral use of estramustine phosphate and amino acids for cancer treatment

INVENTOR(S):

Muggetti, Lorena; Colombo, Paolo; Martini, Alessandro;

Buzzi, Giovanni

PATENT ASSIGNEE(S):

Pharmacia & Upjohn S.p.A., Italy

PCT Int. Appl., 24 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	ENT	NO.		KIND DATE						PPLI	CATI	ON NO	ο.	DATE				
	WO 2001019372					A1 20010322				WO 2000-EP8983					2000		Ø		
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ÃΖ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
			CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	
			HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,	
			SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	
			YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM					
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
			DE,	DK,	ES,	ΓI,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	
			CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG				
PRIO	RITS	APP	LN.	INFO	. :					GB 1	999-:	2196	0	Α	1999	0916			
AB	Αŗ	aren	tera	l fo	rmul	atio:	n fo	r ca	ncer	tre	atme	nt c	ompr	ises	est	ramu	stin	e	

phosphate, a basic amino acid, and a parenterally acceptable carrier or diluent. The formulation can be administered according to a combined chemotherapy regimen in assocn. with one or more chemotherapeutic agents. The formulation enables the estramustine phosphate to be administered with no side effects at the site of injection. Prepn. of estramustine phosphate N-methyl-glucamine salt in admixt. with arginine (estramustine phosphate/meglumine/arginine in a molar ratio 1:1:2) was presented. 204005-46-9, SU 5416

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combined chemotherapy; formulations for parenteral use of estramustine phosphate and basic amino acids for cancer treatment)

RN 204005-46-9 CAPLUS

> 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 11 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:208081 CAPLUS

DOCUMENT NUMBER:

134:242666

TITLE:

IT

CN

Formulations for parenteral use of estramustine

phosphate and sulfoalkyl ether cyclodextrins Muggetti, Lorena; Colombo, Paolo; Martini, Alessandro;

INVENTOR(S):

Buzzi, Giovanni Pharmacia & Upjohn S.P.A., Italy

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                                         KIND DATE
                                                                                  APPLICATION NO.
                                                                                                                  DATE
                                          ----
                                                     -----
         WO(2001019339
                        D19339 A1 20010322 WO 2000-EP7680 20000803
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
                                         __A1
                        CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
                 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GB, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
                        CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                                                           GB 1999-21958
                                                                                                             A 19990916
```

A pharmaceutical formulation which comprises a parenterally acceptable carrier or diluent, estramustine phosphate and a sulfoalkyl ether cyclodextrin. The formulation can be administered according to a combined chemotherapy regimen in assocn. with one or more chemotherapeutic agents. The formulation also enables estramustine phosphate to be administered with no side effects at the site of injection. A soln. contq.

estramustine phosphate and sulfobutyl ether .beta.-cyclodextrin (1:4.2) was formulated.

IT 204005-46-9, SU 5416

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (parenteral formulations contg. estramustine phosphates and sulfoalkyl ether cyclodextrins and other chemotherapeutic agents)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 12 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:208080 CAPLUS

DOCUMENT NUMBER:

134:242665

TITLE:

CN

Formulations for parenteral use of estramustine phosphate with improved pharmacological properties

INVENTOR(S):

Muggetti, Lorena; Colombo, Paolo; Martini, Alessandro;

Buzzi, Giovanni

PATENT ASSIGNEE(S):

Pharmacia & Upjohn S.P.A., Italy

SOURCE:

PCT Int. Appl., 21 pp. CODEN: PIXXD2

DOCUMENT TYPE:

I TYPE: Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE ____ _____ WO 2000-EP7679 20000803 20010322 WO 2001019338 A1 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG GB 1999-21954 A 19990916 PRIORITY APPLN. INFO.: A pharmaceutical formulation which comprises a parenterally acceptable carrier or diluent, estramustine phosphate, a sulfoalkyl ether cyclodextrin and human albumin. The formulation can be administered according to a combined chemotherapy regimen in assocn. with one or more chemotherapeutic agents. The formulation also enables the estramustine phosphate to be administered with no side effects at the site of injection. A soln. contg. estramustine phosphate (Estracyt), sulfobutyl ether .beta.-cyclodextrin, and human albumin (1:1:0.21) was formulated. IT 204005-46-9, SU 5416 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (parenteral formulations contg. estramustine phosphates and sulfoalkyl ether cyclodextrins and human albumins and chemotherapeutic agents)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 13 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:114989 CAPLUS

DOCUMENT NUMBER:

134:168371

TITLE:

Formulations for parenteral use of estramustine

phosphate and albumin

INVENTOR(S):

Muggetti, Lorena; Colombo, Paolo; Martini, Alessandro;

Buzzi, Giovanni

PATENT ASSIGNEE(S):

Pharmacia & Upjohn S.p.A., Italy

SOURCE:

PCT Int. Appl., 14 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND						DATE			A	PPLI	CATI	ON N	0.	DATE					
WO 2001010446 WO 2001010446					A2 20010215 A3 20010525				M	0803									
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
						DK,													
		HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,		
		LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,		
		SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,		
		YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM						
	RW:	GH,	GM,	ΚE,	LS,	MW,	ΜŻ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,		
						FR,													
																	-		
RITY	CF, CG, CI, CM, GA, SITY APPLN. INFO.:												A 19990809						

PRIORITY APPLN. INFO.:

GB 1999-18779 A 19990809
IT 1999-MI1998 A 19990927
AB A pharmaceutical formulation which comprises a parenterally acce

AB A pharmaceutical formulation which comprises a parenterally acceptable carrier or a diluent and estramustine phosphate in admixt. with human albumin, wherein the wt. ratio of estramustine phosphate to human albumin is from about 1:5 to about 1:0.3. The formulation can be administered according to a combined chemotherapy regimen in assocn. with one or more chemotherapeutic agents. The formulation also enables estramustine phosphate to be administered with no side effects at the side of injection. A parenteral soln. contained N-Me glucamine salt of estramustine phosphate 30 mg, and human albumin 25 mg/mL (1:0.8 wt. ratio resp.).

IT 204005-46-9, Su 5416

RN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(formulations for parenteral use of estramustine phosphate and albumin) 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:917070 CAPLUS

DOCUMENT NUMBER: 136:214530

TITLE: The t(8;22) in chronic myeloid leukemia fuses BCR to

FGFR1: transforming activity and specific inhibition

of FGFR1 fusion proteins

AUTHOR(S): Demiroglu, Asuman; Steer, E. Joanna; Heath, Carol;

Taylor, Kerry; Bentley, Mark; Allen, Steven L.; Koduru, Prasad; Brody, Judith P.; Hawson, Geoffrey; Rodwell, Robyn; Doody, Mary-Lou; Carnicero, Fernando; Reiter, Andreas; Goldman, John M.; Melo, Junia V.;

Cross, Nicholas C. P.

CORPORATE SOURCE: Department of Haematology, Imperial College School of

Medicine, Hammersmith Hospital, London, UK

SOURCE: [Blood (2001), 98(13), 3778-3783

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal LANGUAGE: English

AR This report describes 2 patients with a clin. and hematol. diagnosis of chronic myeloid leukemia (CML) in chronic phase who had an acquired t(8;22)(p11;q11). Anal. by fluorescence in situ hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) indicated that both patients were neg. for the BCR-ABL fusion, but suggested that the BCR gene was disrupted. Further FISH indicated a breakpoint within fibroblast growth factor receptor 1 (FGFR1), the receptor tyrosine kinase that is known to be disrupted in a distinctive myeloproliferative disorder, most commonly by fusion to ZNF198. RT-PCR confirmed the presence in both cases of an in-frame mRNA fusion between BCR exon 4 and FGFR1 exon 9. Expression of BCR-FGFR1 in the factor-dependent cell line Ba/F3 resulted in interleukin 3-independent clones that grew at a comparable rate to cells transformed with ZNF198-FGFR1. The growth of transformed cells was inhibited by the phosphatidylinositol 3-kinase inhibitor LY294002, the farnesyltransferase inhibitors L744832 and manumycin A, the p38 inhibitors SB202190 and SB203580 but not by the MEK inhibitor PD98059. The growth of BaF3/BCR-FGFR1 and BaF3/ZNF198-FGFR1 was not significantly inhibited by treatment with STI571, but was inhibited by SU5402, a compd. with inhibitory activity against FGFR1. Inhibition with this compd. was assocd. with decreased phosphorylation of ERK1/2 and BCR-FGFR1 or ZNF198-FGFR1, and was dose dependent with an inhibitory conca. of 50% of approx. 5 mu-M. As expected, growth of BaF3/BCR-ABL was inhibited by STI571 but not by SU5402. The study demonstrates that the BCR-FGFR1 fusion may occur in patients with apparently typical CML. Patients with constitutively active FGFR1 fusion genes may be amenable to treatment with specific FGFR1 inhibitors.

IT **215543-92-3**, SU 5402

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(t(8;22) in chronic myeloid leukemia fuses BCR to FGFR1: transforming

activity and specific inhibition of FGFR1 fusion proteins)
RN 215543-92-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:354377 CAPLUS

DOCUMENT NUMBER:

2001:354377 CF 135:146994

TITLE:

Indolinone tyrosine kinase inhibitors block Kit activation and growth of small-cell lung cancer cells

AUTHOR(S):

Krystal, Geoffrey W.; Honsawek, Sittisak; Kiewlich, David; Liang, Congxin; Vasile, Stefan; Sun, Li;

McMahon, Gerald; Lipson, Kenneth E.

CORPORATE SOURCE:

Departments of Internal Medicine and

Microbiology/Immunology, McGuire Veterans Affairs Medical Center, Virginia Commonwealth University,

Richmond, VA, 23249, USA

SOURCE:

Cancer Research (2001), 61(9), 3660-3668

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal English

LANGUAGE: AB Six indolinone tyrosine kinase inhibitors were characterized for their ability to inhibit Kit kinase and for their effects on the growth of small-cell lung cancer (SCLC) cell lines. All six compds. were potent inhibitors of Kit kinase in a biochem. assay. A homol. model of compd. binding to the ATP-binding site could account for the increased potency caused by the addn. of a propionate moiety to the indolinone core but not that caused by addn. of a chloride moiety. Although all of the compds. tested were potent in the biochem. assay, several exhibited significantly less potency in cellular kinase assays. Their effects on stem cell factor (SCF)-dependent Kit autophosphorylation and SCLC cell growth were also examd. Inhibition of SCF-stimulated Kit activation and cell growth of the H526 cell line was concn. dependent. At concns. that inhibited SCF-stimulated H526 cell growth, there was little effect on insulin-like growth factor-1-stimulated growth, suggesting that these compds. exhibit reasonable selectivity for inhibition of Kit-mediated proliferation.

Higher concns. of the compds. were needed to inhibit serum-stimulated growth. Of the six compds. examd., SU5416 and SU6597 possessed the best cellular potency and, therefore, their effect on the growth of multiple SCLC cell lines in serum-contg. media was examd. In addn. to inhibiting proliferation, these compds. also induced cell death of several SCLC cell lines, but not of normal human diploid fibroblasts, in complete media.

These observations suggest that Kit kinase inhibitors such as these may offer a new approach for inhibiting Kit-mediated proliferation of tumors such as SCLC, gastrointestinal stromal tumors, seminomas, and leukemias.

IT 186611-14-3, SU 6663 186611-56-3, SU 5614 204005-46-9, SU 5416 251356-16-8 251356-18-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological

study)

(indolinone-type tyrosine kinase inhibitors blockade of Kit activation and growth of small-cell lung cancer cells)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm CH}_{
m CH_2-CH_2-CO_2H}$

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 251356-16-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$C1$$
 H
 CH
 N
 CH
 CH_2
 CH_2
 CH_2
 CH_2

RN 251356-18-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

C1

$$H$$
 CH
 H
 Me
 $CH_2-CH_2-CO_2H$

REFERENCE COUNT:

34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 16 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:799778 CAPLUS

DOCUMENT NUMBER:

TITLE:

136:112324 Sequential tumor biopsies in early phase clinical

trials of anticancer agents for pharmacodynamic-

ewaluation

AUTHOR(S): Dowlati, Afshin; Haaga, John; Remick, Scot C.; Spiro,

Timothy P.; Gerson, Stanton L.; Liu, Lili; Berger, Sosamma J.; Berger, Nathan A.; Willson, James K. V.

CORPORATE SOURCE:

Division of Hematology/Oncology, Department of Medicine and Developmental Therapeutics Program, Ireland Cancer Center at University Hospitals of Cleveland and Case Western Reserve University,

Cleveland, OH, 44106, USA

Clinical Cancer Research (2001), 7(10), 2971-2976 SOURCE:

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal

LANGUAGE: English In the setting of target-based anticancer drug development, it is crit. to AB establish that the obsd. preclin. activity can be attributed to modulation of the intended target in early phase trials in human subjects. paradigm of target modulation allows the authors to det. a Phase II or III dose (optimal biochem./biol. modulatory dose) that may not necessarily be the max. tolerated dose. A major obstacle to target-based (often cytostatic) drug development has been obtaining relevant tumor tissue during clin. trials of these novel agents for lab. anal. of the putative marker of drug effect. From 1989 to present, the authors have completed seven clin. trials in which the end point was a biochem. or biol. modulatory dose in human tumor tissues (not surrogate tissue). Eligibility enrollment required that patients have a biopsiable lesion either with computerized tomog. (CT) guidance or direct visualization and consent to sequential (pre and posttreatment) biopsies. A total of 192 biopsies were performed in 107 patients. All but 8 patients had sequential pre and posttreatment biopsies. Seventy-eight (73%) of the 107 patients had liver lesion biopsies. In eight patients, either one or both biopsies contained insufficient viable tumor tissue or no tumor tissue at all for anal. Of a total of 99 patients in whom the authors attempted to obtain paired biopsies, a total of 87 (88%) were successful. Reasons for failure included patient refusal for a second biopsy (n = 2), vasovagal reaction with first biopsy precluding a second biopsy (n = 1), subcapsular

feasible and safe during early phase clin. trials. IT 204005-46-9, SU5416

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sequential human tumor biopsies in early phase clin. trials of

hepatic bleeding (n = 1), and most commonly obtaining necrotic tumor, fibrous, or normal tissue in one of the two sequential biopsies (n = 8). This is the first and largest reported series demonstrating that with adequate precautions and experience, sequential tumor biopsies are

anticancer agents for pharmacodynamic evaluation)

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS 27 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 17 OF 70

ACCESSION NUMBER:

2001:240686 CAPLUS

DOCUMENT NUMBER:

135:2309

TITLE:

Inhibition of vascular endothelial growth factor

receptor signaling leads to reversal of tumor

resistance to radiotherapy

AUTHOR(S):

Geng, Ling; Donnelly, Edwin; McMahon, Gerald; Lin, P.

Charles; Sierra-Rivera, Elaine; Oshinka, Halina;

Hallahan, Dennis E.

CORPORATE SOURCE:

Departments of Radiation Oncology, Vanderbilt

University School of Medicine, Vanderbilt University,

Nashville, TN, 37232, USA

SOURCE:

Cancer Research (2001), 61(6), 2413-2419

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal LANGUAGE: English

Certain refractory neoplasms, such as glioblastoma multiforme (GBM) and melanoma, demonstrate a resistant tumor phenotype in vivo. We obsd. that these refractory tumor models (GBM and melanoma) contain blood vessels that are relatively resistant to radiotherapy. To det. whether the vascular endothelial growth factor receptor-2 (Flk-1/KDR) may be a therapeutic target to improve the effects of radiotherapy, we used the sol. extracellular component of Flk-1 (ExFlk), which blocks vascular endothelial growth factor binding to Flk-1 receptor expressed on the tumor endothelium. Both sFlk-1 and the Flk-1-specific inhibitor SU5416 eliminated the resistance phenotype in GBM and melanoma microvasculature as detd. by both the vascular window and Doppler blood flow methods. Human microendothelial cells and human umbilical vein endothelial cells showed minimal radiation-induced apoptosis. The Flk-1 antagonists sFlk-1 and SU5416 reverted these cell models to apoptosis-prone phenotype. Flk-1 antagonists also reverted GBM and melanoma tumor models to radiation-sensitive phenotype after treatment with 3 Gy. These findings demonstrate that the tumor microenvironment including the survival of tumor-assocd. endothelial cells contributes to tumor blood vessel resistance to therapy.

IT **204005-46-9**, SU 5416

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor vascularization inhibitor; inhibition of VEGF receptor signaling enhances radiation-induced response in tumor blood vessels)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (CA INDEX NAME)

REFERENCE COUNT:

39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 18 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

2001:169669 CAPLUS

134:348.057

TITLE:

The antiangiogenic protein kinase

inhibitors SU5416 and SU6668 inhibit the SCF receptor (c-kit) in a human myeloid leukemia cell line and in

acute myeloid leukemia blasts

AUTHOR(S):

Smolich, Beverly D.; Yuen, Helene A.; West, Kristina A.; Giles, Francis J.; Albitar, Maher; Cherrington,

Julie M.

CORPORATE SOURCE:

SOURCE:

Sugen, South San Francisco, CA, 94080, USA

/Blood (2001), 97(5), 1413-1421 CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER:

American Society of Hematology Journal

DOCUMENT TYPE:

LANGUAGE: English AR

SU5416 and SU6668 are potent antiangiogenic small-mol. inhibitors of receptor tyrosine kinases, including those of the vascular endothelial growth factor and platelet-derived growth factor receptor families. stem cell factor (SCF) receptor, c-kit, is structurally related to these receptors and, although not expressed on mature peripheral blood cells, is expressed in leukemic blasts derived from 60% to 80% of acute myeloid leukemia (AML) patients. The c-kit kinase inhibitory activity of SU5416 and SU6668 was evaluated in MO7E cells, a human myeloid leukemia cell line. Tyrosine autophosphorylation of the receptor, induced by SCF, was inhibited in these cells by SU5416 and SU6668 in a dose-dependent manner (inhibitory concn. of 50% [IC50] 0.1-1 .mu.M). Inhibition of extracellular signal-regulated kinase 1/2 (ERK1/2) phosphorylation, a signaling event downstream of c-kit activation, was also inhibited in a dose-dependent manner. Both compds. also inhibited SCF-induced proliferation of MO7E cells (IC50 0.1 .mu.M for SU5416; 0.29 .mu.M for SU6668). Furthermore, both SU5416 and SU6668 induced apoptosis in a doseand time-dependent manner as measured by the increase in activated caspase-3 and the enhanced cleavage of its substrate poly(ADP-ribose) polymerase. These findings with MO7E cells were extended to leukemic blasts from c-kit+ patients. In patient blasts, both SU5416 and SU6668 inhibited SCF-induced phosphorylation of c-kit and ERK1/2 and induced apoptosis. These studies indicate that SU5416 and SU6668 inhibit biol. functions of c-kit in addn. to exhibiting antiangiogenic properties and suggest that the combination of these activities may provide a novel therapeutic approach for the treatment of AML.

IT **204005-46-9**, SU5416

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(the antiangiogenic protein kinase inhibitors

SU5416 and SU6668 inhibit the SCF receptor (c-kit) in a human myeloid leukemia cell line and in acute myeloid leukemia blasts)

RN 204005-46-9 CAPLUS

H

Jones

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 19 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:905718 CAPLUS

DOCUMENT NUMBER:

136:160779

TITLE:

Semaxanib (SUGEN)

AUTHOR(S): CORPORATE SOURCE: Sakamoto, Kathleen M.

Department of Pedlatncs and Pathology, UCLA School of Medicine, Los Angeles, CA, 90095-1752, USA

SOURCE: IDrugs_(2001), 4-(9), 1061-1067

CODEN: IDRUFN; ISSN: 1369-7056

PUBLISHER:

Current Drugs Ltd.

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

A review. SUGEN (owned by Pharmacia) is developing semaxanib (SU-5416), the lead in a series of small mol. inhibitors of the flk-1 tyrosine kinase receptor (flk-1 RTK), for the potential treatment of solid tumors (via suppression of metastasis and angiogenesis). In July 1999, phase III trials for colorectal and lung cancer were initiated. In Mar. 2001, phase III trials were initiated for the compd. as an addn. to a std. chemotherapy regimen in colorectal cancer; at this time, Pharmacia, as well as the NCI, was conducting clin. studies for numerous other solid and hematol. cancers. By Oct. 2000, oral forms of the compd. were also being evaluated. In July 2000, Pharmacia anticipated US and international filing in 2001. Taiho and SUGEN have agreed a joint development program for SUGEN's angiogenesis inhibitors. In August 1998, the USPTO issued US-05792783 to SUGEN, covering a family of compds., including semaxanib. The patent claims cover the compds. and compn., as well as methods of use in a variety of diseases, including cancer. In August 1998, the USPTO issued US-05792783 to SUGEN, covering a family of compds., including semaxanib. The patent claims cover the compds. and compn., as well as methods of use in a variety of diseases, including cancer.

IT 194413-58-6, Semaxanib

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(semaxanib, an inhibitor of the flk-1 tyrosine kinase receptor, for potential treatment of solid tumors in humans)

RN 194413-58-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 20 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:688215 CAPLUS

DOCUMENT NUMBER:

TITLE:

GI

133:252306 Preparation of indolinones as protein

kinase inhibitors.

INVENTOR(S):

Tang, Peng Cho; Sun, Li; Mcmahon, Gerald; Miller, Todd

Anthony; Shirazian, Shahrzad; Wei, Chung Chen; Harris,

G. Davis, Xiaoyuan, Li; Liang, Congxin

PATENT ASSIGNEE(S):

SOURCE:

Swgen, Inc., USA PCT Int. Appl., 245 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	ND	DATE				APPLI		٥.	DATE								
WO	2000	0567	09	 A	1	2000	0928					 4	20000322					
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA	, BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	
		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES	, FI,	GB,	GD,	GE,	GH,	GM,	HR,	ΗU,	
		ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP	, KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	
•		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX	, NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	
		SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT	, TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	
		ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU	, TJ,	TM							
	RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SL,	SZ	, TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	
		-	-	-		-				, LU,				SE,	BF,	ΒJ,	CF,	
										, NE,								
EP									EP 2000-916622									
	R:							FR,	GB	, GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		•	•	,	LV,	FI,	RO											
PRIORIT	Y APP	LN.	INFO	. :						1999-			-					
										1999-			_					
										1999-			-					
										1999-								
						2000-	US770	04	W	2000	0322							
OTHER SOURCE(S):						PAT :	133:	2523	06									

Searched by Barb O'Bryen, STIC 308-4291

Ι

Title compds., e.g. [I; m, n = 0, 1; Q = (JR11)m; Q1 = (DR6)n; when n = 1, then A, B, D, E, F = C, N; .ltoreq.3 of A, B, D, E, F = N; when m = 1, then G, H, J, K, L = C, N; .gtoreq.1 and .ltoreq.3 of G, H, J, K, L = N; when n = 0, then A = C, N, B, F = C, N, NH, O, S; E = C, N, O, S; when m = O, then G = C, N, H, K, l = C, N, NH, O, S; R1-R13 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy, SH, alkylthiol, aryloxy, amino, etc.; R4R5 or R5R6 or R6R7 or R7R8 = atoms to form a 5-6 membered (hetero)aryl ring; with addnl. provisos], were prepd. Thus, 6-pyridin-3-yl-1,3-dihydroindol-2-one (prepn. given), 4-methoxy-3-thien-2-ylbenzaldehyde, and piperidine were refluxed overnight in EtOH to give 15% 3-(4-methoxy-3-thien-2-ylbenzylidene)-6-pyridin-3-yl-1,3-dihydroindol-2-one. Tested title compds. inhibited HER2 kinase with IC50 = 16.4 .mu.M to .gtoreq.100 .mu.M.

1T 251356-74-8P 295799-29-0P 295799-31-4P 295799-47-2P 295799-51-8P 295799-89-2P 295799-90-5P 295799-97-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of indolinones as protein kinase inhibitors)

RN 251356-74-8 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

$$HO-CH_2-CH_2$$
 $HO-CH_2-CH_2$
 $HO-C$

RN 295799-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-4-[2-[3-(1-methylethyl)phenoxy]ethyl]- (9CI) (CA INDEX NAME)

RN 295799-31-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-4-[2-[3-(1-methylethyl)phenoxy]ethyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

RN 295799-47-2 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-6-(3-pyridinyl)- (9CI) (CA INDEX NAME)

$$H$$
 N
 CH
 H
 N
 Me
 $(CH2)3-NMe2$

RN 295799-51-8 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-6-(2-thienyl)- (9CI) (CA INDEX NAME)

RN 295799-89-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)(4-methoxyphenyl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 295799-90-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethoxyphenyl)(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 295799-97-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-4-[2-[4-(1-methylethyl)phenoxy]ethyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-(9CI) (CA INDEX NAME)

IT 251356-61-3P 251356-63-5P 251356-65-7P 251356-66-8P 251356-67-9P 251356-68-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
 (prepn. of indolinones as protein kinase
 inhibitors)

RN 251356-61-3 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$H$$
 CH
 H
 N
 Me
 $(CH2)3-NMe2$

RN 251356-63-5 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

Br
$$\stackrel{H}{\sim}$$
 CH $\stackrel{H}{\sim}$ Me $(CH2)3-NMe2$

RN 251356-65-7 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 251356-66-8 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-6-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

MeO
$$H$$
 N Me CH Me Me $(CH2)3-NMe2$

RN 251356-67-9 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-6-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

MeO
$$H$$
 N Me CH Me Me $(CH2)3-NMe2$

RN 251356-68-0 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[[4-[3-(dimethylamino)propyl]-3,5-dimethyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$C1$$
 H
 N
 CH
 Me
 $CH_2)_3-NMe_2$

REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 21 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:421132 CAPLUS

DOCUMENT NUMBER:

133:43433

TITLE:

Preparation of 4-aryl-3-(azolylmethylidene)-2-

oxindoles as inhibitors of JNK protein

kinases.

INVENTOR(S): Corbett, Wendy Lear, Luk, Kin-chun; Mahaney, Paige E. F. Hoffmann-La Roche A G., Switz. PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 91 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ------WO-2000035909 20000.622 WO 1999-EP9673 ___ A1 19991209 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG BR 9916223 Α 20010904 BR 1999-16223 19991209 EP 1149093 A1 20011031 EP 1999-966933 19991209 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 6307056 B1 20011023 US 1999-464466
PRIORITY APPLN: INFO:: US 1998-112590P

US 1999-12590P P 19981217 US 1998-112590P P 19981217 US 1999-149028P P 19990816

WO 1999-EP9673 W 19991209

OTHER SOURCE(S):

MARPAT 133:43433

$$R^3$$
 R^3
 R^3

Title compds. [I; A = (substituted) aryl, heteroaryl; R2 = H, halo, OR4, NR6R7, COR4, CO2R4, cyano, NO2, SO2R4, SO2NR6R7, etc.; R3 = H, OR4, COR4, CO2R4, CONR6R7, halo, cyano, NR6R7, perfluoroalkyl, (substituted) alkyl, etc.; R4 = H, (substituted) alkyl, cycloalkyl, heterocyclyl; R6, R7 = H, (substituted) alkyl, cycloalkyl, COR8, CO2R8, SO2R8, etc.; NR6R7 = (substituted) 3-7 membered ring; R8 = H, (substituted) alkyl, aryl, heteroaryl, cycloalkyl; X = N, CH], were prepd. Thus, (Z)-1,3-dihydro-4-iodo-3-[(1H-pyrrol-2-yl)methylene]-2H-indol-2-one (prepn. given) was heated with phenylboronic acid, Pd(OAc)2, Et3N, and tri-O-tolylphosphine in DMF at 100.degree. for 24 h to give 85% (Z)-1,3-dihydro-4-phenyl-3-[(1H-pyrrol-2-yl)methylene]-2H-indol-2-one. Tested I inhibited SAPK with IC5O<0.15 .mu.M.

IT 276251-67-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-aryl-3-(azolylmethylidene)-2-oxindoles as inhibitors of JNK protein kinases)

276251-67-3 CAPLUS RN

2H-Indol-2-one, 5-fluoro-1,3-dihydro-4-(4-hydroxyphenyl)-3-[(3-methyl-1Hpyrrol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS 2 REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 22 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:421131 CAPLUS

DOCUMENT NUMBER:

133:43432

TITLE:

CN

Preparation of 4-alkynyl-3-(pyrrolylmethylene)-2oxoindoles as inhibitors of cyclin-dependent kinases,

in particular CDK2

INVENTOR(S):

Chen, Yi; Corbett, Wendy Lea; Dermatakis, Apostolos;

Liu, Jin-jun; Luk, Kin-chun; Mahaney, Paige E.;

Mischke, Steven-Gregory

PATENT ASSIGNEE(S):

F. Hoffmann-La Roche Ag, Switz.

SOURCE:

PCT Int. Appl., 170 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2000035908	A1 20000622	WO 1999-EP9624	19991208
	AM, AT, AU, AZ, BA,		
DE, DK,	EE, ES, FI, GB, GD,	GE, GH, GM, HR, HU,	ID, IL, IN, IS,
JP, KE,	KG, KP, KR, KZ, LC,	LK, LR, LS, LT, LU,	LV, MA, MD, MG,
	MW, MX, NO, NZ, PL,		
	TR, TT, UA, UG, UZ,		
	TJ, TM		
RW: GH, GM,	KE, LS, MW, SD, SL,	SZ, TZ, UG, ZW, AT,	BE, CH, CY, DE,
DK, ES,	FI, FR, GB, GR, IE,	IT, LU, MC, NL, PT,	SE, BF, BJ, CF,
	CM, GA, GN, GW, ML,		
	A 20010918		19991208
EP 1157019	A1 20011128	EP 1999-963422	19991208
R: AT, BE,	CH, DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
	LT, LV, FI, RO		
	A 20001010	US 1999-464502	19991215

20010626 US 6252086 R1 US 2000-549864 20000414 US 6303793 В1 20011016 US 2000-566054 20000505 PRIORITY APPLN. INFO.: US 1998-112591P P 19981217 US 1999-149073P P 19990816 W 19991208 WO 1999-EP9624 US 1999-464502 A3 19991215

OTHER SOURCE(S): MARPAT 133:43432

GΙ

The title compds. (I) [wherein R1 = H, acyl, carboxy, carbamido, AB (un) substituted (cyclo) alkyl, or heterocyclyl; R2 = H, alkoxy, acyl(oxy), carboxy, carbamido, halogen, NO2, CN, sulfamido, perfluoroalkyl, alkyl, etc.; R3 = H, alkoxy, acyl(oxy), carboxy, carbamido, halogen, CN, amino, perfluoroalkyl, alkyl, etc.; X = N or (un)substituted C] and their intermediates and analogs were prepd. by reaction of alkynes with 4-halo-2-oxoindoles. I inhibit cyclin-dependent kinases (CDKs), esp. CDK2, and are useful as anti-proliferative agents in the treatment or control of cell proliferative disorders, in particular breast and colon tumors. For example, Me 4-pentynoate was coupled with (Z)-4-bromo-1,3-dihydro-3-[(3-methoxy-1H-pyrrol-2-yl)methylene]-5-nitro-2Hindole-2-one (prepn. given) using (Ph3P)2PdCl2 and CuI as catalysts in DMF and TEA to give (Z)-II in 72% yield. In a CDK2 flash plate assay, II inhibited CDK2 by > 90% at concns. of .ltoreq. 1.0 .mu.M. Representative compds. of the invention were tested in cell-based assays against epithelial breast carcinoma line MDA-MB435 and colon carcinoma line SW480 and gave IC50 values of < 3.5 .mu.M and < 1.0 .mu.M, resp. Formulations for tablets, capsules, and injection soln./emulsion prepns. are also included.

IT 275387-68-3P, (Z)-3-[(4-Acetyl-1H-pyrrol-2-yl)methylene]-1,3dihydro-5-fluoro-4-iodo-2H-indol-2-one 275387-99-0P
275388-01-7P 275388-18-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275387-68-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-iodo-, (3Z)- (9CI) (CA INDEX NAME)

RN 275387-99-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-01-7 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-18-6 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

corresponding 4-halo-2-oxoindoles) RN 275387-69-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(tetrahydro-4-hydroxy-2H-pyran-4-yl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-73-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 275387-74-1 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

HC1

RN 275387-77-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-78-5 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

$$\begin{array}{c}
H \\
N \\
C \longrightarrow C
\end{array}$$

$$\begin{array}{c}
H \\
N \\
H
\end{array}$$

$$\begin{array}{c}
H \\
N \\
H
\end{array}$$

● HCl

RN 275388-00-6 CAPLUS
CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3dihydro-4-[-(2S)-2-pyrrolidinylethynyl]-, monohydrochloride, (3Z)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

● HCl

RN 275388-02-8 CAPLUS
CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

● HCl

RN 275388-03-9 CAPLUS
CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,3-dihydro-, monohydrochloride, (3Z)- (9CI) (CA INDEX

NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & H & O & Ac \\ \hline & & & \\ EtNH & & & \\ \hline \end{array}$$

● HCl

RN 275388-04-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(4-hydroxy-4-piperidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

● HCl

RN 275388-10-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & H & O & Me \\ \hline & N & O & Me \\ \hline & Z & & N \\ \hline & EtnH & C \Longrightarrow C & H \end{array}$$

● HCl

RN 275388-19-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HC1

RN 275388-31-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-[(2-hydroxypropyl)amino]-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275388-32-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-(ethylamino)-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-33-5 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(2R)-3-(ethylamino)-2-methyl-2H-pyran-6-yl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-34-6 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-35-7 CAPLUS

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3S,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 23 OF 70 2000:144722 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER:

132:185454

TITLE:

Use of anti-angiogenic agents for inhibiting vessel

wall injury

INVENTOR(S): PATENT ASSIGNEE(S): Brown, Charles L., III; Gorlin, Steve Global Vascular Concepts, Inc., USA

SOURCE:

PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

PRIO

English___

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT	KI	ND	DATE			A	PPLI	CATI	Э.	DATE						
				A2 (20.000302				برين بند بند	W	0 19	99-U	19990824					
WO	2000				_												
	W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
		CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
		IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,
														SE,			
														AM,			
		KZ,	MD,	RU,	TJ,	TM	•	•									
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,
														BF,			
		CI,	CM,	GA,	GN.	GW,~	ML,	MR,	NE,	SN,	TD,	_T.G					
AU	9956	871		Α	1	2000	0314		A	U 19	99-5	6871	-	1999	0824		
	APP					•								1998			
									WO 1	999-	US19	218	W	1999	0824		

- Use of anti-angiogenic agents to inhibit an undesirable response to vessel AB wall injury, including stent neointima, dialysis graft neointima, vascular graft-induced neointima, and the treatment of benign-hypertrophic-scar formation as well as the treatment and passivation of unstable atherosclerotic plaques are provided. The invention provides for the use of catheter-based devices for enhancing the local delivery of anti-angiogenic agents into the endothelial tissues of blood vessels of the living body.
- IT **204005-46-9**, SU5416

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (anti-angiogenic agents for inhibiting vessel wall injury)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (CA INDEX NAME)

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 24 OF 70

ACCESSION NUMBER:

2000:117197 CAPLUS

DOCUMENT NUMBER:

132:166123

TITLE:

3-Methylidenyl-2-indolinone modulators of

INVENTOR(S):

Protein kinase Tang, Peng Cho; Sun, Li; Miller, Todd Anthony; Liang,

Congxin; Tran, Ngoc My; Nguyen, Anh Thi; Nematalla,

Asaad

PATENT ASSIGNEE (-S):

SOURCE:

Sugen, Inc., USA

PCT Int. Appl., 347 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.				KIND I				APPLICATION NO.					DATE				
	WO 2000008202 WO 2000008202					20000217 20000518			WO 1999-US17845 19990804									
	W:	DK, KE, MW,	EE, KG, MX,	ES, KP, NO,	FI, KR, NZ,	GB, KZ, PL,	GD, LC, PT,	GE, LK, RO,	GH, LR, RU,	GM, LS, SD,	HR, LT, SE,	HU, ĽU, SG,	ID, LV, SI,	CN, IL, MD, SK, KG,	IN, MG, SL,	IS, MK, TJ,	JP, MN, TM,	
AU_	RW: 99546	ES, CI,	GM, FI, CM,	FR, GA,	GB, GN,	GR, GW,	IE, ML,	IT, MR,	LU, NE,	MC, SN,	NL, TD,	PT,	SE,	CH, BF,	ВJ,	CF,		
PRIORITY	APPI	Ň.	-NFO					 	US 1 US 1 US 1 US 1	998- 998- 998- 999-	12925 95470 1021 11610 US178	56 DP 78P D7P	A P P P	1998 1998 1998 1999	0804 0805 0928 0115			
OTHER SO GI	URCE	(S):			MAR	PAT	132:	1661:	23							/		

Searched by Barb O'Bryen, STIC

$$R^2$$
 R^3
 A
 N
 O
 R^4
 R^0
 I

Jones

The title compds. (I) [wherein A = C or N; Q = substituted Ph, pyrroly1, or indolyl; R0 = H, alkyl, C(O)R19, or C(O)OR19; R1 = H, (un)substituted alkyl, alkoxy, halo, aryl, (CH2)nOC(0)R19, or C(0)NR19; R2 = H, (cyclo)alkyl, (hetero)aryl, heteroalicyclic, trihalomethyl, alkoxy, halo, sulfamido, C(0)OR19, C(0)R19, NHC(0)OR19, (un)substituted amino, etc.; R3 = H, alkyl, trihalomethyl, alkoxy, aryl(oxy), heteroaryl, heteroalicyclic, OH, halo, sulfamido, C(O)R19, (un)substituted amino, etc.; R4 = H, alkyl, alkoxy, or halo; R19 = H, (cyclo)alkyl, alkenyl, alkynyl, or aryl; n = 1-4] were prepd. as modulators of the activity of receptor tyrosine kinases (RTKs), non-receptor protein tyrosine kinases (CTKs), and serine/threonine protein kinases (STKs). Examples include over 200 syntheses and data from seventeen bioassays. For instance, II was prepd. by a 3-step sequence involving: (1) cyclization and redn. of 2,4-dinitrophenylacetic acid with SnCl2.2H2O in EtOH to form 6-amino-2-oxindole, (2) amidation with AcCl in CH2Cl2, and (3) condensation of the amide with 3,5-diisopropyl-4-methoxybenzaldehyde. II was tested for HER-2 kinase activity (IC50 = 6.4 .mu.M), cellular proliferation activity as measured by the incorporation of bromodeoxyuridine (BrdU) driven by HER-2 (IC50 = 9.1 .mu.M) or EGF (IC50 = 11 .mu.M), and antitumor activity as measured by growth of SKOV3 ovarian carcinoma cells (IC50 = 2.6 .mu.M) or A431 human epidermoid carcinoma cells (IC50 = 2.2 .mu.M). The invention compds. are expected to be useful n the prevention and treatment of protein kinase elated cellular disorders such as cancer, diabetes, hepatic rrhosis, cardiovascular disease, and immunol. disease.

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R831-72-0P 258831-76-4P 258831-77-5P
R31-78-6P 258831-79-7P 258831-80-0P
R1-81-1P 258831-82-2P 258831-84-4P
-87-7P 258831-89-9P 258831-90-2P
P1-3P 258831-92-4P

(Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT or reagent)
ediate; prepn. of 3-methylidenyl-2-indolinones as kinase modulators for the prevention and of cancer, diabetes, hepatic cirrhosis, ular disease, and immunol. disease)

APLUS
(2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-ylethyl ester (9CI) (CA INDEX NAME)
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RN 258831-76-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 258831-77-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$H$$
 CH
 H
 CO_2H
 $HO_2C-CH_2-CH_2$
 He

RN 258831-78-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & O & H \\ \hline & O & CH & N \\ \hline & & \\ HO-CH_2-CH_2-O-C-CH_2-CH_2 & Me \\ \end{array}$$

RN 258831-79-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 258831-80-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$C1$$
 $HO_2C-CH_2-CH_2$
 Me

RN 258831-81-1 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 258831-82-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\text{H}}_{\text{N}}$$
 $^{\text{O}}_{\text{CH}}$ $^{\text{H}}_{\text{N}}$ $^{\text{CO}_{2}\text{H}}_{\text{Me}}$

RN 258831-84-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(6-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 258831-87-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-carboxy-4-methyl- (9CI) (CA INDEX NAME)

Br
$$HO_2C-CH_2-CH_2$$
 Me

RN 258831-89-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(1,2-dihydro-5-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

Me
$$HO_2C-CH_2-CH_2$$
 Me

RN 258831-90-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ N & CH & N \\ HO_2C-CH_2-CH_2 & Me \end{array}$$

RN 258831-91-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 258831-92-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-carboxy-2-[[6-(3-ethoxyphenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

IT 258830-03-4P 258830-04-5P 258830-17-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; as **protein kinase** modulators for the prevention and treatment of cancer, **diabetes**, hepatic cirrhosis, cardiovascular disease, and immunol. disease)

RN 258830-03-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & O \\ \hline & CH & N & Me \\ \hline & HO_2C-CH_2-CH_2 & C-OEt \\ \hline & O & \\ \end{array}$$

RN 258830-04-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & O \\ \hline & CH & N \\ \hline & HO_2C-CH_2-CH_2 \end{array}$$

RN 258830-17-0 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[4-(ethoxycarbonyl)-5-methyl-3-[3-(4methyl-1-piperazinyl)propyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

245036-29-7P 258831-06-0P 258831-07-1P IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (target compd.; prepn. of 3-methylidenyl-2-indolinones as protein kinase modulators for the prevention and treatment of cancer, diabetes, hepatic cirrhosis, cardiovascular disease, and immunol. disease) 245036-29-7 CAPLUS

RN

CN

1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 258831-06-0 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-4-methyl-2-oxo-3Hindol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

C1
$$\frac{H}{Me}$$
 $CH_2-CH_2-CO_2H$

RN 258831-07-1 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H- indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

```
Br CH CH_2-CH_2-CO_2H
```

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IT
     22813-86-1P 215543-92-3P 245036-10-6P
     245036-15-1P 245036-16-2P 245036-17-3P
     245036-28-6P 256657-46-2P 256657-47-3P
     256657-49-5P 256657-51-9P 258829-97-9P
     258829-98-0P 258829-99-1P 258830-00-1P
     258830-01-2P 258830-02-3P 258830-05-6P
     258830-06-7P 258830-07-8P 258830-08-9P
     258830-09-0P 258830-10-3P 258830-11-4P
     258830-12-5P 258830-13-6P 258830-14-7P
     258830-15-8P 258830-16-9P 258830-18-1P
     258830-19-2P 258830-20-5P 258830-21-6P
     258830-22-7P 258830-23-8P 258830-24-9P
     258830-26-1P 258830-28-3P 258830-30-7P
     258830-32-9P 258830-34-1P 258830-36-3P
     258830-37-4P 258830-39-6P 258830-41-0P
     258830-43-2P 258830-45-4P 258830-47-6P
     258830-49-8P 258830-51-2P 258830-53-4P
     258830-55-6P 258830-57-8P 258830-59-0P
     258830-61-4P 258830-63-6P 258830-64-7P
     258830-65-8P 258830-66-9P 258830-68-1P
     258830-69-2P 258830-70-5P 258830-71-6P
     258830-72-7P 258830-73-8P 258830-74-9P
     258830-75-0P 258830-76-1P 258830-77-2P
     258830-78-3P 258830-79-4P 258830-83-0P
     258830-88-5P 258830-92-1P 258830-93-2P
     258830-94-3P 258830-95-4P 258830-96-5P
     258830-97-6P 258830-98-7P 258830-99-8P
     258831-00-4P 258831-01-5P 258831-02-6P
     258831-04-8P 258831-05-9P 258831-08-2P
     258831-09-3P 258831-11-7P 258831-12-8P
     258831-13-9P 258831-14-0P 258831-15-1P
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (target compd.; prepn. of 3-methylidenyl-2-indolinones as
        protein kinase modulators for the prevention and
        treatment of cancer, diabetes, hepatic cirrhosis,
        cardiovascular disease, and immunol. disease)
     22813-86-1 CAPLUS
RN
     2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI)
                                                                    (CA INDEX
CN
     NAME)
```

RN 215543-92-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 245036-10-6 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

MeO
$$HO_2C-CH_2-CH_2$$

RN 245036-15-1 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(4-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 245036-16-2 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 245036-17-3 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 245036-28-6 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H \\ H \\ CH \\ \hline \\ CH_2 - CH_2 \\ \hline \\ C - NH - CH_2 - CH_2 \\ \hline \\ O \\ \end{array}$$

RN 256657-46-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 256657-47-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

Br
$$HO_2C-CH_2-CH_2$$
 Me

RN 256657-49-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

MeO
$$HO_2C-CH_2-CH_2$$
 Me

RN 256657-51-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[6-(3-ethoxyphenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 258829-97-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[6-(4-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{H} & \text{O} \\ \text{HO}_2\text{C}-\text{CH}_2-\text{CH}_2 \end{array}$$

RN 258829-98-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 4-(ethoxycarbonyl)-2-[[6-(4-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{H} & \text{O} \\ \text{H} & \text{N} \\ \text{CH} & \text{H} \\ \text{HO}_2\text{C} - \text{CH}_2 - \text{CH}_2 \\ \text{O} \end{array}$$

RN 258829-99-1 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 258830-00-1 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

OMe
$$H = CH$$

$$HO_2C - CH_2 - CH_2$$

$$C - OET$$

$$O$$

RN 258830-01-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl- (9CI) (CA INDEX NAME)

$$C1$$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$

RN 258830-02-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

C1

$$HO_2C-CH_2-CH_2$$
 $C-OEt$
 O

RN 258830-05-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & O \\ \hline & H & C - OEt \\ \hline & HO_2C-CH_2-CH_2 & Me \end{array}$$

RN 258830-06-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-morpholinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 258830-07-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

MeNH-S

O

CH

N

O

CH

N

Me

CH

N

Me

CH

N

Me

CH

N

Me

Me

RN 258830-08-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-[3-(dimethylamino)propyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

MeO
$$\frac{H}{N}$$
 O $\frac{H}{N}$ Me $\frac{H}{N}$ Me $\frac{H}{N}$ Me $\frac{H}{N}$ O $\frac{H}{N}$ Me $\frac{H}{N}$ O $\frac{H}{N}$ Me $\frac{$

RN 258830-09-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-4-[3-(4-morpholinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 258830-10-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 258830-11-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-morpholinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 258830-12-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & &$$

RN 258830-13-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[4-(ethoxycarbonyl)-5-methyl-3-[3-(4-morpholinyl)propyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)

RN 258830-14-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-6-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(1-pyrrolidinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & H & O \\ H & N & O \\ \hline O & CH & Me \\ \hline & (CH_2)_3 & C-OEt \\ N & O & \\ \end{array}$$

RN 258830-15-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-4-[3-(1-pyrrolidinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & (CH_2)_3 & C-OEt \\ N & O & \\ \end{array}$$

RN 258830-16-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[4-(ethoxycarbonyl)-5-methyl-3-[3-(1-pyrrolidinyl)propyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & CH & N \\ \hline & CH & N \\ \hline & CH & N \\ \hline & C - OEt \\ \hline & N & O \\ \end{array}$$

RN 258830-18-1 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(1-pyrrolidinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & &$$

RN 258830-19-2 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-morpholinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
- CH_2
 CH

RN 258830-20-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(1-pyrrolidinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & CH & N & Me \\ \hline & (CH_2)_3 & C - OEt \\ \hline & N & O \\ \end{array}$$

RN 258830-21-6 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-[3-(dimethylamino)propyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$H_2N-S$$
 O
 $Me_2N-(CH_2)_3$
 $C-OEt$
 O
 O

RN 258830-22-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[3-[3-(dimethylamino)propyl]-4-(ethoxycarbonyl)-5-methyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C$$
 HO_2C
 HO_2C
 HO_2C
 HO_2C
 HO_2C
 $CHOET$

RN 258830-23-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-[3-(dimethylamino)propyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
- CH_2 Me_2N - $(CH_2)_3$ C - OEt

RN 258830-24-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-4-(2-hydroxyethyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
- CH_2
 CH

RN 258830-26-1 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-[3-(dimethylamino)propyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 258830-28-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-[3-(dimethylamino)propyl]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H & Me \\
MeNH-S & & CH & N & Me \\
\hline
O & Me2N-(CH2)3 & CO2H
\end{array}$$

RN 258830-30-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

RN 258830-32-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline H & C - OEt \\ \hline MeO & HO_2C-CH_2-CH_2 & Me \\ \end{array}$$

RN 258830-34-1 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\stackrel{N}{\stackrel{}}}$$
 $\stackrel{O}{\stackrel{C}{\stackrel{}}}$ $\stackrel{O}{\stackrel{H}{\stackrel{}}}$ $\stackrel{O}{\stackrel{C}{\stackrel{}}}$ $\stackrel{C}{\stackrel{O}{\stackrel{}}}$ $\stackrel{C}{\stackrel{O}{\stackrel{}}}$ $\stackrel{C}{\stackrel{O}{\stackrel{}}}$ $\stackrel{C}{\stackrel{O}{\stackrel{}}}$

RN 258830-36-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(6-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

RN 258830-37-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

Br
$$HO_2C-CH_2-CH_2$$
 Me

RN 258830-39-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

RN 258830-41-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[5-(aminosulfonyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$H_2N-S$$
 H_2N-S
 $H_2N-C-OEt$
 $H_2N-C-OEt$

RN 258830-43-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

RN 258830-45-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[5-[(dimethylamino)sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline Me_2N-S & & CH & C-OEt \\ \hline O & HO_2C-CH_2-CH_2 & Me \end{array}$$

RN 258830-47-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-5-[[(1-methylethyl)amino]sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{i-PrNH-S} \\ & & \\$$

RN 258830-49-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-51-2 CAPLUS

CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
- CH_2
HN

(CH₂)₃-NMe₂

RN 258830-53-4 CAPLUS

CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-5-methoxy- (9CI) (CA INDEX NAME)

MeO
$$\frac{H}{N}$$
 O $\frac{H}{N}$ $\frac{H}{N}$ $\frac{H}{N}$ $\frac{H}{N}$

RN 258830-55-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-methyl-3-[(3-methyl-1H-indol-2-yl)methylene]-(9CI) (CA INDEX NAME)

RN 258830-57-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$H_2N-S$$
 O
 H_2N-S
 O
 Me

RN 258830-59-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo- (9CI) (CA INDEX NAME)

RN 258830-61-4 CAPLUS

CN lH-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

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$$\begin{array}{c|c} & & & \\ &$$

RN 258830-63-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-2-oxo-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 258830-62-5 CMF C19 H14 N2 O3

CM 2

CRN 110-89-4 CMF C5 H11 N

RN 258830-64-7 CAPLUS

CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-(9CI) (CA INDEX NAME)

RN 258830-65-8 CAPLUS

CN 2H-Indol-2-one, 5-acetyl-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 258830-66-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & \\ H_2N-S & \\ \vdots & \vdots & \\ O & \\ \end{array}$$

RN 258830-68-1 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

$$H_{2N}$$
 CH
 N
 H

RN 258830-69-2 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-70-5 CAPLUS

CN 2H-Indol-2-one, 6-chloro-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 258830-71-6 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1, 3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 258830-72-7 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-(1H-indol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 258830-73-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-methyl- (9CI) (CA INDEX NAME)

RN 258830-74-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 258830-75-0 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene](9CI) (CA INDEX NAME)

RN 258830-76-1 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene]-(9CI) (CA INDEX NAME)

RN 258830-77-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-methyl-3-[(3-methyl-1H-indol-2-yl)methylene](9CI) (CA INDEX NAME)

RN 258830-78-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-5-[(1H-indol-2-ylmethylene)amino]- (9CI) (CA INDEX NAME)

RN 258830-79-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-83-0 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(3-methyl-1H-indol-2-yl)methylene](9CI) (CA INDEX NAME)

$$H_{2N}$$
 H_{2N}
 H_{2N}
 H_{2N}
 H_{2N}
 H_{2N}

RN 258830-88-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N,N-dimethyl-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-92-1 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

$$C1$$
 $HO_2C-CH_2-CH_2$

RN 258830-93-2 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} CH \\ \end{array} \begin{array}{c} H \\ N \\ \end{array} \begin{array}{c} H$$

RN 258830-94-3 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 258830-95-4 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-5-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

Me
$$HO_2C-CH_2-CH_2$$

RN 258830-96-5 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(6-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 258830-97-6 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 258830-98-7 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N,N-dimethyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 258830-99-8 CAPLUS

CN 2H-Indol-2-one, 3-[[3-[3-(dimethylamino)propyl]-4,5,6,7-tetrahydro-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 258831-00-4 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ N & CH & O \\ & & \\ CH_2-CH_2-C-NH_2 \end{array}$$

RN 258831-01-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[4,5,6,7-tetrahydro-3-[3-(4-morpholinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 258831-02-6 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-methyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H \\ & N \\ \hline & CH \\ \hline & CH_2-CH_2-C-NHMe \\ \end{array}$$

RN 258831-04-8 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-5-[[(1-methylethyl)amino]sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

$$i-PrNH-S$$
 H
 O
 $HO_2C-CH_2-CH_2$

RN 258831-05-9 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-6-(4-morpholinyl)-2-oxo-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ \hline & N & CH & H \\ \hline & HO_2C-CH_2-CH_2 & \end{array}$$

RN 258831-08-2 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 258831-09-3 CAPLUS

CN 1H-Indole-3-propanamide, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4,5,6,7-tetrahydro-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 258831-11-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H \\ \hline & CH & N \\ \hline & HO_2C-CH_2-CH_2 & Me \end{array}$$

RN 258831-12-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 258831-13-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(6-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$C1$$
 H
 CH
 N
 $HO_2C-CH_2-CH_2$
 Me

RN 258831-14-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-5-methyl-2-oxo-3H-indol-3ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

Me
$$\begin{array}{c} H \\ N \\ CH \\ \end{array}$$

$$\begin{array}{c} H \\ N \\ \end{array}$$

RN 258831-15-1 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-5-methoxy-2-oxo-3H-indol-3ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 25 OF 70

ACCESSION NUMBER:

2001:83373 CAPLUS

DOCUMENT NUMBER:

135:86674

TITLE:

The angiogenesis inhibitor SU5416 has long-lasting

effects-on-vascular-endothelial-growth-factor_receptor

phosphorylation and function

AUTHOR(S):

Mendel, Dirk B.; Schreck, Randall E.; West, David C.; Li, Guangmin; Strawn, Laurie M.; Tanciongco, Sheila S.; Vasile, Stefan; Shawver, Laura K.; Cherrington,

CORPORATE SOURCE:

SOURCE:

Sugen, Pric., South San Francisco, CA, 94080, USA Clinical Cancer Research (2000), 6(12), 4848-485

ch (2000), 6(12), 4848-4858

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal English

LANGUAGE:

505416, a selective inhibitor of the tyrosine kinase activity of the vascular endothelial growth factor (VEGF) receptor Flk-1/KDR, is currently in Phase III clin. trials for the treatment of advanced malignancies. In cellular assays, SU5416 inhibits the VEGF-dependent mitogenic/proliferative response of human umbilical vein endothelial cells (HUVECs). In tumor xenograft models, SU5416 inhibits the growth of tumors from a variety of origins by inhibiting tumor angiogenesis. In three different human tumor xenograft models, infrequent (once or twice a week)



administration of SU5416 is efficacious despite the fact that it has a short plasma half-life (30 min), which suggests that SU5416 has long-lasting inhibitory activity in vivo. The goal of the present study was to det. the basis for the prolonged activity of SU5416. The results indicate that a short (3 h) exposure to $5 \, .mu.M \, SU5416$ (to mimic plasma levels of the compd. as measured in patients who were receiving ${\tt SU5416}$ therapy) produced long-lasting (at least 72 h) inhibition of the VEGF-dependent proliferation of HUVECs in culture, which indicate that SU5416 has long-lasting inhibitory activity in vitro as well as in vivo. SU5416 treatment of HUVECs did not affect surface expression of Flk-1/KDR or the affinity of the receptor for VEGF. Instead, the durability of the in vitro activity of SU5416 was shown to be attributable to its long-lasting ability to specifically inhibit VEGF-dependent phosphorylation of Flk-1/KDR and subsequent downstream signaling, although SU5416 is not an irreversible inhibitor of Flk-1/KDR tyrosine kinase The long-lasting inhibition of cellular responses to VEGF was attributable to the accumulation of SU5416 in cells, as shown using radiolabeled compd., such that inhibitory cellular concns. of SU5416 are maintained long after the removal of the compd. from the medium. The long-lasting inhibitory activity of SU5416 in vitro is consistent with the finding that SU5416 has demonstrated evidence of biol. activity in clin. studies when administered twice a week despite a short plasma half-life.

204005-46-9, SU5416 ΙT

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiogenesis inhibitor SU5416 has long-lasting effects on vascular endothelial growth factor receptor phosphorylation and function in relation to antitumor effects)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS 48 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 26 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:500184 CAPLUS

DOCUMENT NUMBER:

133:234344

TITLE:

CN

DoMCoSAR: A Novel Approach for Establishing the

Docking Mode That Is Consistent with the

Structure-Activity Relationship. Application to

HIV-1 Protease Inhibitors and VEGF Receptor

Tyrosine Kinase Inhibitors

AUTHOR(S):

Vieth, Michal; Cummins, David J.

CORPORATE SOURCE:

Lilly Research Laboratories, Eli Lilly and Company,

Indianapolis, IN, 46285, USA

SOURCE:

Journal of Medicinal Chemistry (2000), 43(16),

3020-3032

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB DoMCoSAR is a novel approach for statistically detg. the docking mode that is consistent with a structure-activity relationship. The approach establishes the binding mode for the compds. in a chem. series with the assumption that all mols. exhibit the same binding mode. It involves three stages. In the first stage all mols. that belong to a given chem. series are docked to the active site of the protein target. The only bias used in the docking at this stage involves the location of the protein binding site. Coordinates of the common substructure (CS) that results from the unbiased docking are then clustered to establish the major substructure docking modes. In the second stage all mols. are docked to the major docking modes (MDMs) with constraints based on the common substructure. The third stage generates, for the major docking modes, interaction-based descriptors that include electrostatic, VDW, strain, and solvation contributions. The problem of docking mode evaluation is now reduced to the question of which descriptor set is more predictive. establish a quant. comparison of the descriptor sets assocd. with the major docking modes, we use 50 instances of random 4-fold cross-validation. For each 4-fold cross-validation the predictive squared correlation coeff. (R2) is computed. T-Tests are applied to establish significance of the differences in mean R for one docking mode vs. another. We test the methodol. on two test cases: HIV-1 protease inhibitors (Holloway et al. J. Med. Chem. 1995, 38, 305-317) and vascular endothelial growth factor (VEGF) receptor tyrosine kinase oxoindoles (Sun et al. J. Med. Chem. 1998, 41, 2588-2603). For both test cases there is statistically significant preference for the binding mode consistent with the x-ray structure. The appeal of this methodol. is that researchers gain the objectivity of statistical justification for the selected docking mode. The methodol. is relatively insensitive to subtle variations of the protein structure that include, but are not limited to, side chain and small backbone rearrangement during binding. In addn., predictive models that result from the approach can be used to further optimize chem. series.

IT 15966-93-5 186610-94-6 186611-29-0 186611-37-0 186611-48-3 204005-46-9 204005-54-9 293302-24-6 293302-25-7 293302-26-8 293302-27-9

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(VEGF kinase-inhibitor; DoMCoSAR - novel approach for establishing docking mode that is consistent with structure-activity relationship with application to HIV-1 protease inhibitors and VEGF receptor tyrosine kinase inhibitors)

RN 15966-93-5 CAPLUS

CN

1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-94-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-54-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 293302-24-6 CAPLUS

CN 2H-Indol-2-one, 3-[[3-(3,3-dihydroxypropyl)-4-methyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H$$
 O
 OH
 $HO-CH-CH_2-CH_2$
 Me

RN 293302-25-7 CAPLUS

CN 2H-Indol-2-one, 3-[[4-(3,3-dihydroxypropyl)-3-methyl-1H-pyrrol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & O \\ \hline & H & N & O \\ \hline & CH & CH_2-CH_2-CH-OH \\ \hline \end{array}$$

RN 293302-26-8 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-6-fluoro-1,3-dihydro- (9CI) (CA INDEX NAME)

293302-27-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-CN methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS 45 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 27 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:860816 CAPLUS

DOCUMENT NUMBER:

134:141334

TITLE:

Biokramsformation of the anti-angiogenic compound

Antonian, Lida; Zhang, Hongbing; Yang, Cheng; Wagner, AUTHOR(S): Greg; Shawver, Laura K.; Shet, Manjunath; Ogilvie,

Brian; Madan, Ajay; Parkinson, Andrew

CORPORATE SOURCE:

SOURCE:

AB

SUGEN, Inc., South San Francisco, CA, 94080, USA Drug Metabolism and Disposition 42000), 28(12),

1505-1512

CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER:

American Society for Pharmacology and Experimental

Therapeutics

DOCUMENT TYPE:

LANGUAGE:

Journal English

SU5416 [3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one) an inhibitor of VEGF (vascular endothelial growth factor) receptor tyrosine kinase, Flk-1/KDR (fetal liver kinase 1/kinase insert domain-contg. receptor), also known as VEGF receptor 2 (VEGFR2) is in advanced clin. trials for treatment of AIDS-related Kaposi's sarcoma and colorectal and nonsmall cell lung cancers. Since this chem. class has not been studied previously with therapeutic intent, the present study was designed to investigate the in vitro metab. of SU5416 by mouse, rat, dog, monkey, and human liver microsomes and to identify the major metabolites of SU5416. An HPLC procedure was developed and validated to resolve and quantify SU5416 and its metabolites. To evaluate the in vitro metab. of SU5416, pooled liver microsomes from mice, rats, dogs, monkeys, and humans were incubated with SU5416 (25 .mu.M) in the presence of an NADPH-generating system. In the presence of NADPH, mouse, rat, dog, monkey, and human liver microsomes converted SU5416 to at least 12, 9, 9, 7, and 6 polar metabolites, resp. Microsomal metab. of SU5416 showed marked species differences in the levels of different metabolites formed. The overall rate of SU5416 metab. by liver microsomes from the species examd. followed the rank order: monkey .gtoreq. mouse .apprxeq. rat > dog > human. Two major metabolites of SU5416 were

identified, a hydroxymethyl deriv. of SU5416 (M12) and a carboxylic acid deriv. of SU5416 (M6), by spectroscopic methods and comparison with authentic compds. Both of these oxidative metabolites were further metabolized in vivo through glucuronidation. The metabolic fate of SU5416 in microsomes from various species as well as data from in vivo biotransformation in the rat are discussed.

ΙT **204005-46-9**, SU5416

> RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC

(biotransformation of anti-angiogenic compd. SU5416)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(CA INDEX NAME)

ΙT 280748-38-1, SU 6689 280748-39-2, SU 6595

280748-41-6, SU 9838 324047-04-3 324047-05-4

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative) (biotransformation of anti-angiogenic compd. SU5416)

RN 280748-38-1 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5hydroxy- (9CI) (CA INDEX NAME)

280748-39-2 CAPLUS RN

1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O \\ \hline \\ CH & N \\ \hline \\ Me \\ \end{array}$$

RN 280748-41-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-(hydroxymethyl)-3-methyl-1H-pyrrol-2yl]methylene]- (9CI) (CA INDEX NAME)

$$CH$$
 CH
 CH
 CH
 CH

RN 324047-04-3 CAPLUS

CN .beta.-D-Glucopyranosiduronic acid, [5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-pyrrol-2-yl]methyl (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 324047-05-4 CAPLUS

CN .beta.-D-Glucopyranuronic acid, 1-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-pyrrole-2-carboxylate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

REFERENCE COUNT:

19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 28 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:431391 CAPLUS

DOCUMENT NUMBER:

133:246860

TITLE:

Indolinone derivatives inhibit constitutively activated KIT mutants and kill neoplastic mast cells

AUTHOR(S):

Ma, Yongsheng; Carter, Eric; Wang, Xiaomei; Shu,

CORPORATE SOURCE:

Chang; McMahon, Gerald; Longley, B. Jack
Department of Dermatology, College of Physicians and

Surgeons, Columbia University, New York, NY, 10032,

USA

SOURCE:

Journal of Investigative Dermatology (2000), 114(2),

Searched by Barb O'Bryen, STIC 308-4291

392-394

CODEN: JIDEAE; ISSN: 0022-202X

PUBLISHER:
DOCUMENT TYPE:

Blackwell Science, Inc.

DOCUMENT TYPE: LANGUAGE:

Journal English

AB Mastocytosis is a neoplastic disease caused at least in part by somatic mutations of the c-KIT protooncogene resulting in constitutive activation of its protein product, KIT, the receptor tyrosine kinase for stem cell factor. KIT stimulates mast cell proliferation and prevents apoptosis of neoplastic mast cells. To develop potential therapies for mastocytosis we used indolinones, small mols. that inhibit tyrosine kinases. Four indolinone derivs. (SU4984, SU6663, SU6577, and SU5614) inhibited wild-type KIT, but variably inhibited constitutively activated KIT mutants. SU4984, SU6577, and SU5614 were effective against KIT with juxtamembrane activating mutations, whereas only SU6577 could suppress KIT contg. either juxtamembrane or kinase domain activating mutations. Furthermore, SU4984, SU6577, and SU5614 killed neoplastic mast cells expressing a juxtamembrane-mutated KIT, whereas SU4984 and SU6577 killed neoplastic mast cells expressing KIT bearing a kinase domain mutation. These data show a direct correlation between inhibition of constitutively activated KIT and the death of neoplastic mast cells, and point to specific tyrosine kinase inhibitors as a potential therapy aimed directly at a cause of mastocytosis.

IT 186611-14-3, SU 6663 186611-56-3, SU 5614

251356-17-9, SU 6577

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(indolinone derivs. inhibit activated KIT mutants and kill neoplastic mast cells)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$H$$
 CH
 CH
 $CH_2-CH_2-CO_2H$

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 251356-17-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-6-methoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19

L65 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:64436 CAPLUS

132:342905 DOCUMENT NUMBER:

AUTHOR(S):

Inhibition of transforming activity of the ret/ptcl TITLE:

oncoprotein by a 2-indolinone derivative

Lanzi, Cinzia; Cassinelli, Giuliana; Pensa, Tiziana; Cassinis, Marco; Gambetta, Romolo A.; Borrello, Maria

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

G.; Menta, Ernesto; Pierotti, Marco A.; Zunino, Franco

Division of Experimental Oncology B, Istituto CORPORATE SOURCE:

Nazionale Tumori, Milan, 20133, <u>Italy</u> International Journal of Cancer (2000), 85(3), 384-390 SOURCE:

CODEN: IJCNAW; ISSN: 0020-7136

Wiley-Liss, Inc. PUBLISHER:

DOCUMENT TYPE: Journal English LANGUAGE:

AΒ Ret-derived oncogenes are frequently and specifically expressed in thyroid tumors. In contrast to the ret receptor, ret oncoproteins are characterized by ligand-independent tyrosine-kinase activity and tyrosine phosphorylation. In this study, novel synthetic arylidene 2-indolinone compds. were evaluated as inhibitors of the ret/ptcl tyrosine kinase. Four compds. inhibited ret/ptc1 activity in immunokinase assay (IC50 27-42 .mu.M) including one (1,3-dihydro-5,6-dimethoxy-3-[(4-hydroxyphenyl) methylene]-2H-indol-2-one) (Cpd I) that selectively inhibited the anchorage-independent growth of NIH3T3 transformants expressing the ret/ptcl gene (NIH3T3ptcl cells). Following exposure to Cpd I, the transformed phenotype of NIH3T3ptc1 cells was reverted, within 24 h, to a normal fibroblast-like morphol. in adherent-cell culture. In these cells, the constitutive tyrosine phosphorylation of ret/ptcl, of the transducing adaptor protein shc and of a series of co-immunopptd. peptides became much reduced, as demonstrated by immunopptn./Western-blot analyses. Data presented provide addnl. evidence that ret/ptcl is directly implicated in malignant transformation, and demonstrate the ability of Cpd I to interfere in the signal transduction pathway constitutively activated by the ret/ptcl oncoprotein. These results confirm the interest of the arylidene 2-indolinone class of tyrosine-kinase inhibitors as tools for the study of ret signaling and the control of cell proliferation in retand ret/ptcs-assocd. diseases. IT

269730-08-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of transforming activity of ret/ptcl oncoprotein by 2-indolinone derivs.)

269730-08-7 CAPLUS RN

2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-5,6-dimethoxy-CN (9CI) (CA INDEX NAME)

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 30 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:509842 CAPLUS

DOCUMENT NUMBER: 133:348326

TITLE:

Targeting angiogenesis inhibits tumor infiltration and expression of the pro-invasive protein SPARC

AUTHOR(S): Vajkoczy, Peter; Menger, Michael D.; Goldbrunner, Roland; Ge, Shugang; Annie, T.; Fong, T.; Vollmar,

Brigitte; Schilling, Lothar; Ullrich, Axel; Hirth, K. Peter; Tonn, Jorg C.; Schmiedek, Peter; Rempel, Sandra

CORPORATE SOURCE: Department of Neurosurgery. Klinikum Mannheim,

University of Heidelberg, Mannheim, D-68167, Germany International Journal of Cancer (2000), 87(2), 261-268 SOURCE:

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

The solid growth of high-grade glioma appears to be critically dependent on tumor angiogenesis. It remains unknown, however, whether the diffuse infiltration of glioma cells into healthy adjacent tissue is also dependent on the formation of new tumor vessels. Here, the authors analyze the relation between tumor angiogenesis and tumor $^{\prime\prime}$ cell infiltration in an exptl. glioma model. C6 cells were implanted into the dorsal skinfold chamber of nude mice, and tumor angiogenesis was monitored by intravital fluorescence videomicroscopy. Glioma infiltration was assessed by the extent of tumor cell invasion into the adjacent chamber tissue and by expression of SPARC, a cellular marker of glioma invasiveness. To test the hypothesis that glioma angiogenesis and glioma infiltration are codependent, the authors assessed tumor infiltration in both the presence and the absence of the angiogenesis inhibitor SU5416. SU5416 is a selective inhibitor of the VEGF/Flk-I signal-transduction pathway, a crit. pathway implicated in angiogenesis. Control tumors demonstrated both high angiogenic activity and tumor cell invasion accompanied by strong expression of SPARC in invading tumor cells at the tumor-host tissue border. SU5416-treated tumors demonstrated reduced vascular d. and vascular surface in the tumor periphery accompanied by marked inhibition of glioma invasion and decreased SPARC expression. direct effect of SU5416 on glioma cell motility and invasiveness was excluded by in vitro migration and invasion assays. These results suggest a crucial role for glioma-induced angiogenesis as a prerequisite for diffuse tumor invasion and a possible therapeutic role for anti-angiogenic compds. as inhibitors of both solid and diffuse infiltrative tumor growth. **204005-46-9**, SU5416

IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(targeting angiogenesis inhibits tumor infiltration and expression of pro-invasive protein SPARC using VEGF/Flk-I signal-transduction pathway inhibitor SU5416)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro(9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS 21 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 31 OF 70

ACCESSION NUMBER:

2000:459469 CAPLUS

DOCUMENT NUMBER:

133:144316

TITLE:

Development of SU5416, a selective small molecule inhibitor of VEGF receptor tyrosine kinase activity,

as an anti-angiogenesis agent

AUTHOR(S):

Mendel, Dirk B.; Laird, A. Douglas; Smolich, Beverly D.; Blake, Robert A.; Liang, Congxin; Hannah, Alison L.; Shaheen, Raymond M.; Ellis, Lee M.; Weitman, Steve; Shawver, Laura K.; Cherrington, Julie M. SUGEN, Inc., South San Francisco, CA, 94080, USA

CORPORATE SOURCE:

Anti-Cancer Drug Design (2000), 15(1), 29-41

SOURCE:

CODEN: ACDDEA; ISSN: 0266-9536

PUBLISHER:

Oxford University Press Journal; General Review

DOCUMENT TYPE:

English

LANGUAGE: A review with over 60 refs. Angiogenesis, or the sprouting of new blood AB vessels, is a central process in the growth of solid tumors. For many cancers, the extent of vascularization of a tumor is a neg. prognostic indicator signifying aggressive disease and increased potential for metastasis. Recent efforts to understand the mol. basis of tumor-assocd. angiogenesis have identified several potential therapeutic targets, including the receptor tyrosine kinases for the angiogenic factor vascular endothelial growth factor (VEGF). Here we review the approach taken at SUGEN, Inc. to discover and develop small mol. inhibitors of receptor tyrosine kinases as anti-angiogenic agents. We focus on SU5416, a selective inhibitor of VEGF receptors that is currently in clin. development for the treatment of advanced malignancies. Its biochem., biol. and pharmacol. properties are reviewed and clin. implications discussed.

204005-46-9, SU5416 IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (VEGF receptor tyrosine kinase inhibitors SU5416 development as anti-angiogenesis agent)

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (CA INDEX NAME)

REFERENCE COUNT:

60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:352846 CAPLUS

DOCUMENT NUMBER:

133:232264

TITLE:

The role of vascular endothelial growth factor (VEGF)

in AIDS-related Kaposi's sarcoma

AUTHOR(S): CORPORATE SOURCE: Arasteh, Keikawus; Hannah, Alison

Auguste-Viktoria-Krankenhaus, Berlin, D-12157, Germany

SOURCE:

Oncologist (2000) 5 (Suppl. 1), 28-31 CODEN: OCOLF6; ISSN: 1083-7159

PUBLISHER:

AlphaMed Press

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

A review with 33 refs. Kaposi's sarcoma (KS) is the most common

neoplasm assocd. with human immunodeficiency virus-1 (HIV-1) infection. KS involves the skin and mucous membranes as

well as other organs and can lead to tumor-assocd. edema and ulcerations. Despite therapy with highly active antiviral agents, most patients with HIV-1-related KS eventually develop disseminated disease. In the treatment of KS, a strong rationale exists for the use of agents that inhibit vascular endothelial growth factor (VEGF). Angiogenesis appears to be an important feature of this disease, and recent exptl. studies have demonstrated the role of VEGF and its receptors in the pathogenesis of KS. Thus, therapeutic agents that target the VEGF pathway may be an effective strategy in reducing the tumor growth and edema assocd. with KS. Phase I study results with SU5416, a synthetic low mol.-wt. inhibitor of the VEGF-Flk-1/KDR receptor tyrosine kinase, demonstrate that this agent is well tolerated. Preliminary results show that in a majority of patients with autoimmune deficiency syndrome (AIDS)-related disease, SU5416 clearly has biol. activity (it flattens, shrinks, or dissolves lesions and reduces or resolves edema) or stabilizes the disease. Angiogenesis inhibition with SU5416 is a promising therapeutic approach in treating patients with KS, and further clin. evaluation is currently under

204005-46-9, SU5416 ΙT

way.

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(role of vascular endothelial growth factor (VEGF) in AIDS -related Kaposi's sarcoma and treatment with SU5416)

204005-46-9 CAPLUS RN

> 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 33 OF 70 CAPLUS COPYRIGHT 2002 ACS 1999:725101 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

132:30444

TITLE:

Inhibition of angiogenesis by blocking activation of

the vascular endothelial growth factor receptor 2 leads to decreased growth of neurogenic sarcomas Angelov, Lilyana; Salhia, Bodour; Roncari, Luba;

Page 226

McMahon, Gerald; Guha, Abhijit

Division of Neurosurgery, Toronto Western Hospital, CORPORATE SOURCE:

University of Toronto, Toronto, ON, M5T 2S8, Can. Cancer Research (1999), 59(21), 5536-5541

SOURCE:

CODEN: CNREA8; ISSN: 0008-5472

AACR Subscription Office PUBLISHER:

DOCUMENT TYPE: Journal English LANGUAGE:

AUTHOR(S):

Neurogenic sarcomas are incurable, common malignant human peripheral nerve tumors subject to local recurrence and systemic metastasis. In this study, the vascularity, vascular endothelial growth factor (VEGF) expression, and effects of inhibiting VEGF receptor on growth of neurogenic sarcomas were examd. Vascularization and VEGF expression were 6.4- and 15-fold higher in tumors than in normal nerves. The small mol. inhibitor (SU5416) of VEGF receptor 2 had no effect on neurogenic sarcoma cell lines in vitro, but the growth of a human tumor explant xenograft model was reduced by 54.8% compared to vehicle. Redn. in tumor growth was due to decreased tumor angiogenesis, leading to redn. of tumor cell proliferation and increased apoptosis. Inhibiting VEGF function may therefore be a useful adjuvant therapy for neurogenic sarcomas.

204005-46-9, SU5416 ΙT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiogenesis inhibition by VEGF2 blocking leads to decreased growth of neurogenic sarcomas)

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS 69 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:725076 CAPLUS

DOCUMENT NUMBER:

132:44604

TITLE:

Antiangiogenic therapy targeting the tyrosine kinase receptor for vascular endothelial growth factor receptor inhibits the growth of colon cancer liver metastasis and induces tumor and endothelial cell

apoptosis

AUTHOR(S):

Shaheen, Raymond M.; Davis, Darren W.; Liu, Wenbiao; Zebrowski, Brian K.; Wilson, Michael R.; Bucana, Corazon D.; McConkey, David J.; McMahon, Gerald;

Ellis, Lee M.

CORPORATE SOURCE:

Departments of Surgical Oncology, Anderson Cancer Center, The University of Texas M. D., Houston, TX,

77030, USA

SOURCE:

Cancer Research (1999), 59(21), 5412-5416

CODEN: CNREA8; ISSN: 0008-5472

Searched by Barb O'Bryen, STIC 308-4291

PUBLISHER: AACR Subscription Office

DOCUMENT TYPE: Journal LANGUAGE: English

AB Increased vascular endothelial growth factor (VEGF) expression is assocd. with colon cancer metastases. We hypothesized that inhibition of VEGF receptor activity could inhibit colon cancer liver metastases. BALB/c mice underwent splenic injection with CT-26 colon cancer cells to generate metastases. Mice received daily i.p. injections of vehicle, tyrosine kinase inhibitor for Flk-1/KDR (SU5416) or tyrosine kinase inhibitor for VEGF, basic fibroblast growth factor, and platelet-derived growth factor receptors (SU6668). SU5416 and SU6668 resp. inhibited metastases (48.1% and 55.3%), microvessel formation (42.0% and 36.2%), and cell proliferation (24.4% and 27.3%) and increased tumor cell (by 2.6- and 4.3-fold) and endothelial cell (by 18.6- and 81.4-fold) apoptosis (P < 0.001). VEGF receptor inhibitors increased endothelial cell apoptosis, suggesting that VEGF may serve as an endothelial survival factor.

IT **204005-46-9**, SU 5416

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiangiogenic therapy targeting VEGF receptor tyrosine kinase inhibits liver metastasis of colon cancer and induces tumor and endothelial cell apoptosis)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 15

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:65738 CAPLUS

DOCUMENT NUMBER:

130:246450

TITLE:

\$05416 is a potent—and selective inhibitor of the

vascular endothelial growth factor receptor

(Flk-1/KDR) that inhibits tyrosine kinase catalysis, tumor vascularization, and growth of multiple tumor

types

AUTHOR(S):

Fong, T. Annie T.; Shawver, Laura K.; Sun, Li; Tang, Cho; App, Harald; Powell, T. Jeff; Kim, Young H.; Schreck, Randall; Wang, Xueyan; Risau, Werner; Ullrich, Axel; Hirth, K. Peter; McMahon, Gerald

CORPORATE SOURCE:

SUGEN, Inc., South San Francisco, CA, 94080, USA Cancer Res. (1999), 59(1), 99-106

SOURCE:

CODEN: CNREA8; ISSN: 0008-5472

of human endothelial cells without inhibiting the growth of a variety of

PUBLISHER:

AACR Subscription Office

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB SU5416, a novel synthetic compd., is a potent and selective inhibitor of the Flk-1/KDR receptor tyrosine kinase that is presently under evaluation in Phase I clin. studies for the treatment of human cancers. SU5416 was shown to inhibit vascular endothelial growth factor-dependent mitogenesis

Jones

tumor cells in vitro. In contrast, systemic administration of SU5416 at nontoxic doses in mice resulted in inhibition of s.c. tumor growth of cells derived from various tissue origins. The antitumor effect of SU5416 was accompanied by the appearance of pale white tumors that were resected from drug-treated animals, supporting the antiangiogenic property of this agent. These findings support that pharmacol. inhibition of the enzymic activity of the vascular endothelial growth factor receptor represents a novel strategy for limiting the growth of a wide variety of tumor types. 204005-46-9, SU 5416

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SU5416: selective inhibitor of Flk-1/KDR receptor tyrosine kinase, tumor vascularization and growth)

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS 54 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2002 ACS L65 ANSWER 36 OF 70

ACCESSION NUMBER:

2000:117816 CAPLUS

DOCUMENT NUMBER:

133:37825

TITLE:

ΙT

CN

Inhibition of tumor growth, angiogenesis, and

microcirculation by the novel Flk-1 inhibitor SU5416

as assessed by intravital multifluorescence

videomicroscopy

AUTHOR(S):

SOURCE:

Vajkoczy, Peter; Menger, Michael D.; Vollmar,

Brigitte; Schilling, Lothar; Schmiedek, Peter; Hirth,

K. Peter; Ullrich, Axel; Fong, T. Annie T.

Department of Neurosurgery, Klinikum Mannheim, CORPORATE SOURCE:

University of Heidelberg, Mannheim, D-68167, Germany

Neoplasia (New York) (1999), 1(1), 31-41 CODEN: NEOPFL; ISSN: 1522-8002

Stockton Press PUBLISHER:

Journal

DOCUMENT TYPE: English

LANGUAGE: Vascular endothelial growth factor (VEGF) plays a fundamental role in mediating tumor angiogenesis and tumor growth. The direct effect of SU5416, a novel small-mol. inhibitor of the Flk-1-mediated signal transduction pathway of VEGF, on tumor angiogenesis and microhemodynamics of an exptl. glioblastoma was investigated by intravital multifluorescence videomicroscopy. SU5416 treatment suppressed tumor growth. In parallel, SU5416 demonstrated a potent antiangiogenic activity, resulting in redn. of both the total and functional vascular d. of the tumor microvasculature, which indicates an impaired vascularization as well as perfusion failure in the treated tumors. This malperfusion was not compensated for by changes in vessel diam. or recruitment of nonperfused vessels. Analyses of the tumor microcirculation revealed microhemodynamic changes after angiogenesis blockade, such as a higher red cell velocity and blood flow in remnant tumor vessels than in controls. The results demonstrate that the novel antiangiogenic concept of targeting the tyrosine kinase of Flk-1/KDR by means of a small-mol. inhibitor represents an efficient strategy for controlling growth and progression of angiogenesis-dependent tumors.

ΙT **204005-46-9**, SU 5416

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of glioblastoma growth, angiogenesis, and microcirculation by tyrosine kinase inhibitor SU5416)

RN 204005-46-9 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

REFERENCE COUNT:

25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1998:747592 CAPLUS

DOCUMENT NUMBER: TITLE:

Preparation of 3-(hetero)arylmethylidene-2-indolinone

derivatives as modulators of protein

kinase activity for use in treating cancer.

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald; Shawver,

Laura Kay; Hirth, Klaus Peter

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 269 pp. CODEN: PIXXD2

Patent

DOCUMENT TYPE:

LANGUAGE:

English

2

130:3771

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	** <u>*</u>	APPLICATION NO. DATE
W@ 9850356	A11-9981112	WO 1998-US9017 19980507
W: AL, AM,	AT, AU, AZ, BA, B	BB, BG, BR, BY, CA, CH, CN, CH, CZ, DF
DK, EE,	ES, FI, GB, GE, C	GH, GM, GW, HU, ID, II, IS, IP KE KC
KP, KR,	KZ, LC, LK, LR, I	LS, LT, LU, LV, MD, MG, MK, MN, MW, MX
NO, NZ,	PL, PT, RO, RU, S	SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT
UA, UG,	UZ, VN, YU, ZW, A	AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
KW: GH, GM,	KE, LS, MW, SD, S	SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
CM CA	GB, GR, TE, TT, T GN, ML, MR, NE, S	LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
AU 9876842	A1 10001127	AU 1998-76842 19980507
EP 984930	A1 20000315	EP 1998-924746 19980507
R: AT. BE.	CH DE DK EG E	EP 1998-924/46 19980507
IE, FI	OH, BE, BR, ES, F	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
US 6316429	B1 20011113	US 1998-74621 19980507
JP 2002511852		
		US 1998-99721 19980619
US 6313158	B1 20011106	US 1998-100854 19980619
US 6133305	A 20001017	US 1998-161046 19980925
US 2001056094	A1 20011227	US 2000-482198 20000112
US 2001007033		US 2000-516948 20000301
US 2002026053	A1 20020228	US 2001-916331 20010730

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PRIORITY APPLN. INFO.:
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US 1997-45838P 19970507 P US 1997-46868P 19970508 Ρ US 1997-49324P Ρ 19970611 US 1997-50412P Ρ 19970620 US 1997-50413P Ρ 19970620 Ρ 19970620 US 1997-50977P Ρ 19970919 US 1997-59336P Ρ 19970919 US 1997-59381P Ρ 19970919 US 1997-59384P US 1997-59544P P 19970919 US 1997-59677P Ρ 19970919 US 1997-59971P Ρ 19970925 US 1997-60194P Ρ 19970926 WO 1998-US9017 W 19980507 A1 19980619 US 1998-99721 A3 19980925 US 1998-161046 B1 20000301 US 2000-516948

OTHER SOURCE(S):

MARPAT 130:3771

$$\begin{array}{c|c}
R^{3} & R^{2} \\
R^{4} & A^{1} \\
A^{2} & A^{1} \\
R^{5} & A^{4} & N \\
R^{1} & R^{6}
\end{array}$$

Title compds. [I; A1-A4 = C, N; when any of A1-A4 = N, then the corresponding R3-R6 = null; R1 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclyl, trihalomethylcarbonyl, OH, CO2H, trihalomethylsulfonyl, etc.; R2 = H, alkyl, cycloalkyl, aryl, heteroaryl, heteroalicyclyl, halo; R3-R6 = H, alkyl, trihalomethyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclyl, OH, SH, alkoxy, aryloxy, amino, phosphonyl, guanidinyl, NO2, halo, (iso)cyanato, etc.; R3R4 or R4R5 or R5R6 = cycloalkyl, aryl, heteroaryl, heteroalicyclyl, OCH2O, OCH2CH2O; Q = specified (substituted) (hetero)aryl; Z = O, S], were prepd. Thus, 3-(4-imidazolylmethylidenyl)-4,6-dimethyl-2-indolinone inhibited CDK2 with IC50 = <0.78 .mu.M.

IT 15966-93-5 186611-30-3 186611-31-4 186611-33-6 186611-34-7 186611-37-0 215536-87-1 215536-88-2 215536-91-7 215537-01-2 215537-24-9 215537-79-4 215543-92-3 215543-93-4 215543-94-5 215543-95-6 215543-96-7 215543-97-8

Ι

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of **protein kinase** activity for use in treating cancer)

RN 15966-93-5 CAPLUS

CN

1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ Br & & \\ Br & & \\ Me & & \\ Et & & \\ \end{array}$$

RN 215543-92-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-93-4 CAPLUS

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\stackrel{N}{\longrightarrow}}$$
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RN 215543-96-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2002 ACS

1

ACCESSION NUMBER:

1998:147306 CAPLUS

DOCUMENT NUMBER:

128:204803

TITLE:

Indolinone combinatorial libraries and related

products and methods for the treatment of disease

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald; Hirth, Klaus

Peter; Shawver, Laura Kay; et al.

PATENT ASSIGNEE(S):

Sugen, Inc., USA; Tang, Peng Cho; Sun, Li; McMahon,

Gerald

SOURCE:

PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAI	ENT					DATE			A	PPLI	CATI	ои ис	٥.	DATE				
WO 9807695 A1 19980226 WO 1997-US14736 19970820																		
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PRIORITY APPLN. INFO.:
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                                                            A3 19970820
                                           US 1997-915366
                                           WO 1997-US14736 W 19970820
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OTHER SOURCE(S):

AΒ

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MARPAT 128:204803

Ι

The invention relates to indolinone derivs. capable of modulating, regulating, and/or inhibiting protein kinase signal transduction. The compds. are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK protein kinase can be obtained by adding chem. substituents to the 3-[(indole-3-yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. Indolinone compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosol. indolinone compds. that are tyrosine kinase inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepd. by combinatorial condensation of certain (un) substituted indolinones with aldehydes at the 3-position. I gave complete inhibition of MET kinase at chimeric MET receptors in vitro. 203988-42-5p, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone 203988-54-9P, 3-[(3,4-Dibromo-2methylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone 203988-64-1P 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2indolinone 203988-74-3P, 3-[(3,4-Dibromo-2-methylpyrrol-5-

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yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203988-84-5P, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203988-94-7P, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-
(morpholinosulfonyl) -2-indolinone 203989-04-2P,
3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-
indolinone 203989-05-3P, 3-[[2,4-Dimethyl-3-
(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5,7-dibromo-2-indolinone
203989-08-6P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-
[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5,7-dibromo-2-indolinone
203989-14-4P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203989-17-7P,
3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-
[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-iodo-2-indolinone
203989-24-6P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203989-27-9P,
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(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-
5-[(methylamino)sulfonyl]-2-indolinone 203989-52-0P,
3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203989-56-4P
  3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-
[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203989-65-5P
  3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-
(morpholinosulfonyl) -2-indolinone 203989-68-8P,
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[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-(morpholinosulfonyl)-2-
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(\verb|ethoxycarbonyl|) \verb|pyrrol-5-yl|| methylidenyl|] -5-(2-chloroethyl) -2-indolinone
203989-78-0P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-
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203990-08-3P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
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203990-28-7P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
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203990-38-9P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
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yl)methylidenyl]-5,7-dibromo-2-indolinone 203991-72-4P,
3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone
203991-82-6P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-bromo-4-
methyl-2-indolinone 203991-92-8P, 3-[(2,4-Dimethylpyrrol-5-
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203992-02-3P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-12-5P
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yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone 203994-35-8P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5,7-dibromo-2-indolinone 203994-53-0P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203994-72-3P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
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3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
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yl]methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203995-36-2P
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3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203995-57-7P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203995-66-8P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203995-75-9P, 3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-
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nyl]-2-indolinone 203995-84-0P, 3-[[2-(Ethoxycarbonyl)-4-
(methoxycarbonyl)-3-methylpyrrol-5-yl]methylidenyl]-5-(morpholinosulfonyl)-
2-indolinone 203995-93-1P, 3-[[2-(Ethoxycarbonyl)-4-
(\texttt{methoxycarbonyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 2 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \\ \texttt{methoxycarbonyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{methylpyrrol} - 5 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 5 - (2 - \texttt{chloroethyl}) - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 3 - \texttt{yl}] - 3 - \texttt{yl}] \\ \texttt{methylidenyl}] - 3 - \texttt{yl}] -
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204005-38-9P 204005-39-0P 204005-46-9P
 204005-54-9P 204005-56-1P 204005-58-3P
 204005-59-4P
RL: BAC (Biological activity or effector, except adverse); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
       (prepn. and testing of indolinone combinatorial library as
       protein kinase inhibitors)
 203988-42-5 CAPLUS
 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-
 yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)
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RN 203988-54-9 CAPLUS

RN

CN

CN

2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-

dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203988-64-1 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203988-74-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203988-84-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203988-94-7 CAPLUS

CN Morpholine, 4-[[3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203989-04-2 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 H
 CH
 H
 N
 Me

RN 203989-05-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-08-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-14-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & \\ \hline & CH & N \\ \hline & Me & C-OEt \\ \hline & \\ & O \end{array}$$

RN 203989-17-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-24-6 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & Me \\ Br & & CH & N & Me \\ & Me & C-OEt & || & O & Me \\ & & & O & Me \\ & &$$

RN 203989-27-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-35-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-40-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-52-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-56-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-65-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-68-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-75-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2 \xrightarrow{\text{H}} O \xrightarrow{\text{H}} N \text{Me}$$

$$CH \xrightarrow{\text{N}} Me$$

$$C = OEt$$

$$O$$

RN 203989-78-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-88-2 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203989-98-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline I & CH & N & Me \\ \hline \end{array}$$

RN 203990-08-3 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline N & CH & Me \\ \hline Me & Me & Et \\ \end{array}$$

RN 203990-18-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203990-28-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203990-38-9 CAPLUS

CN Morpholine, 4-[[3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203990-48-1 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline C1CH_2-CH_2 & CH & Me \\ \hline \end{array}$$

RN 203991-62-2 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 203991-72-4 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203991-82-6 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203991-92-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203992-02-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203992-12-5 CAPLUS

CN Morpholine, 4-[[3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203992-22-7 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203994-35-8 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ Br & & \\ Br & & \\ &$$

RN 203994-53-0 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline CH & CH & CH_2-C-OMe \\ \hline \\ O & CH_2-C-OMe \\ \hline \end{array}$$

RN 203994-72-3 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-chloro-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

Br
$$MeO-C$$
 $CH_2-C-OMe$

RN 203994-91-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-11-3 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-2-oxo-5-[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-26-0 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-36-2 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 203995-39-5 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-48-6 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline N & O & H & \\ \hline CH & N & C-OEt \\ \hline MeO-C & Me \\ \hline O & \\ \end{array}$$

RN 203995-57-7 CAPLUS

CN 1H-Pyrrole-2, 4-dicarboxylic acid, 5-[(5-bromo-1, 2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-66-8 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-75-9 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-84-0 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-93-1 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 203996-03-6 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203996-13-8 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203996-23-0 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203996-33-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203996-43-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203996-53-6 CAPLUS

CN Morpholine, 4-[[3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203996-63-8 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204003-90-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C$$
 HO_2C
 HO_2C
 HO_2C
 HO_2C
 HO_2C

RN 204003-91-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C$$
 H
 CH
 H
 N
 Et

RN 204003-96-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C$$
 HO_2C
 HO_2C
 HO_2C
 HO_2C
 HO_2C

RN 204003-97-4 CAPLUS

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$

RN 204004-29-5 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2N}$$
 H_{2N}
 H_{2

RN 204004-86-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-amino-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ H_2N & & O \\ Me & CH_2-CH_2-C-OMe \end{array}$$

RN 204004-92-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{C1} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 204004-94-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & N & O & \\ \hline & Me & CH_2-CH_2-C-OMe \end{array}$$

RN 204005-03-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & N & O & \\ \hline & CH & N & \\ \hline & CH_2-CH_2-C-OMe & \\ \hline \end{array}$$

RN 204005-21-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,2,4-trimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 204005-38-9 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ H_2N & CH & N \end{array}$$
 Me Et

RN 204005-39-0 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

Me

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

204005-54-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-CN methyl- (9CI) (CA INDEX NAME)

204005-56-1 CAPLUS RN

2H-Indol-2-one, 5-amino-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-CN dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline H_2N & CH & \\ \hline \end{array}$$

RN204005-58-3 CAPLUS

2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

RN 204005-59-4 CAPLUS

2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-CN methyl- (9CI) (CA INDEX NAME)

ANSWER 39 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1997:640690 CAPLUS

DOCUMENT NUMBER:

127:314804

CODEN: PIXXD2

TITLE:

Assays for KDR/FLK-1 receptor tyrosine kinase

inhibitors, and use of the inhibitors for treatment of

vasculogenesis- and angiogenesis-related diseases-Hirth, Klaus-P.; McMahon, Gerald; Shawver, Laura K.

INVENTOR(S):

PATENT ASSIGNEE(S):

Sugen, Inc., USA PCT Int. Appl., 65 pp.

SOURCE:

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.				KIND DATE			APPLICATION NO.				ο.	DATE					
	WO	9734920		A	A1 19970925		WO 1997-US3378 19970304						0304					
		W:	AL,	AM,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CU,	CZ,	EE,	GE,	GH,
							KG,											
			MN,	MX,	NO,	NZ,	PL,	RO,	RU,	SG,	SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	UZ,
							BY,							•	·	•	·	•
		RW:	GH,	ΚE,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,
							MC,											
			ML,	MR,	ΝE,	SN,	TD,	TG										
•	ΑU	9720	667		A	1	1997	1010		A	U 19	97-20	0667		1997	0304		
PRIORITY APPLN. INFO.:							US 1996-621734 1996032					0321						
					1	WO 1	997-1	US33'	78		1997	0304						

AB Processes are disclosed for the identification of compds. and pharmaceutical compns. capable of selectively and potently inhibiting KDR/FLK-1 tyrosine kinase signal transduction in order to inhibit vasculogenesis and/or angiogenesis. The invention also relates to compds. and compns. identified using the methods of the invention and the use thereof for the treatment of disease relating to inappropriate vasculogenesis and/or angiogenesis. The invention provides an assay cascade comprised of several "filter steps" of increasing selectivity which identify a limited subset of candidate compds. affecting the VEGF receptor on the mol. level.

Jones

204005-46-9, SU 5416 ΙT

RL: BAC (Biological activity or effector, except adverse);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(KDR/FLK-1 receptor tyrosine kinase inhibitor identification assay, and use of compds. for treatment of vasculogenesis- and

angiogenesis-related diseases)

204005-46-9 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 40 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1997:140244 CAPLUS

DOCUMENT NUMBER:

126:139901

TITLE:

CN

Indolinone compounds capable of modulating tyrosine

kinase signal transduction

INVENTOR(S):

Tang, Peng Cho; Sun, Li; Mcmahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE						
MO FOR MOTHE	Δ1 19961219	9 WO 1996-US8903 19960605						
WOL JOHOLLO	AU AZ BB. BG.	G, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IL,						
TS. JP.	KG. KP. KR. KZ.	LK, LR, LS, LT, LV, MD, MG, MK, MN, MX,						
NO. NZ.	PI. RO. RU. SG.	G, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM,						
AZ, BY	,,,							
RW: KE, LS,	MW, SD, SZ, UG,	G, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,						
IE, IT,	LU, MC, NL, PT,	C, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,						
MR. NE.	SN. TD. TG							
US 5880141	A 19990309	09 US 1995-485323 19950607 19 CA 1996-2192797 19960605						
CA 2192797	AA 19961219	.9 CA 1996-2192797 19960605						
AU 9660441	Al 19961230	19961230 AU 1996-60441 19960605						
AU 706597	B2 19990617	17						
EP 769947	A1 19970502	D2 EP 1996-918093 19960605						
EP 769947	B1 20010502)2						
R: AT, BE,	CH, DE, DK, ES,	S, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL,						
PT, SE		40050605						
BR 9606410	A 19971230	BR 1996-6410 19960605						
JP 10504323	T2 19980428	28 JP 1996-501363 19960605						
EP 934931	A2 19990813	EP 1999-103667 19960605						
EP 934931	A3 19991020	20						
		S, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,						
	LT, LV, FI	1000 150565 10060605						
JP 2000026412	A2 2000012	25 JP 1999-159567 19960605						
AT 200863	E 2001051	15 AT 1996-918093 19960605						
ES 2159741	T3 2001101	16 ES 1996-918093 19960605						
JP 3231044	B2 2001111	19 JP 1997-501363 19960605						

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NO 9605377
                            19970212
                       Α
                                           NO 1996-5377
                                                             19961213
PRIORITY APPLN. INFO.:
                                        US 1995-485323
                                                         A 19950607
                                        EP 1996-918093
                                                         A3 19960605
                                        JP 1997-501363
                                                         A3 19960605
                                        WO 1996-US8903
                                                         W 19960605
OTHER SOURCE(S):
                         MARPAT 126:139901
AB
     The present invention relates to org. mols. capable of modulating tyrosine
     kimase signal transduction in order to regulate, modulate and/or inhibit
     abnormal cell proliferation. Representatives of the 5 different classes
     of compds. described are SU 4932 [3-(2-chloro-4-hydroxybenzylidenyl)-2-
     indolinone], SU 4312 [3-(4-dimethylaminobenzylidenyl)-2-indolinone], SU
     5416 {3-[(2,4-dimethylpyrrol-5-yl)methylene]-2-indolinone}, SU 5204
     [3-(2-ethoxybenzylidenyl)-2-indolinone], and SU 4942 [3-(4-
     bromobenzylidenyl)-2-indolinone]. Diseases which these compds. and their
     pharmaceutically acceptable prepns. may be effective against include
     arthritis, hepatic cirrhosis, diabetic nephropathy and
     psoriasis.
ΙT
     15966-93-5P, SU 5408 186610-93-5P, SU 5404
     186610-94-6P, SU 5406 186611-14-3P, SU 5402
     186611-15-4P, SU 5403 186611-16-5P, SU 5405
     186611-17-6P, SU 5407 186611-29-0P, SU 5453
     186611-30-3P, SU 5454 186611-31-4P, SU 5455
     186611-32-5P, SU 5456 186611-33-6P, SU 5459
     186611-34-7P, SU-5460-186611-37-0P, SU-5463
     186611-39-2P, SU 5465 186611-48-3P, SU 5477
     186611-49-4P, SU 5478 186611-50-7P, SU 5479
     186611-54-1P, SU 5613 186611-56-3P, SU 5614
     186611-66-5P, SU 5625 186611-67-6P, SU 5626
     204005-46-9P, SU 5416
     RL: BAC (Biological activity or effector, except adverse); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of indolinones capable of modulating tyrosine kinase signal
        transduction)
RN
     15966-93-5 CAPLUS
     1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-
CN
     ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)
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RN 186610-93-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI)
(CA INDEX NAME)

Jones

RN 186610-94-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
 $^{\rm O}$ $^{\rm H}$ $^{\rm N}$ $^{\rm CH}$ $^{\rm CH}$

RN 186611-15-4 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 CAPLUS

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

09/716332

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-32-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & & O \\ \hline & MeO-C & CH_2-C-OMe \\ \hline & O & \\ \hline & O & \\ \end{array}$$

RN 186611-34-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-49-4 CAPLUS

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 CAPLUS

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & C & Me \\ \hline & CH_2 & \\ \end{array}$$

RN 186611-54-1 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

C1 CH N Me

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-66-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 H
 O
 CH
 H
 N
 Me

RN 186611-67-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 H
 O_1
 O_2
 O_3
 O_4
 O_4
 O_4
 O_4
 O_5
 O_6
 O_6

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 41 OF 70 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1996:746204 CAPLUS

DOCUMENT NUMBER:

126:18783

TITLE:

Substituted indolylmethylene-oxindole analogs as typosime kinase inhibitors

INVENTOR(S):

Battistini, Carlo; Ballinari, Dario; Ermoli, Antonella; Penco, Sergio; Vioglio, Sergio

Pharmacia S.P.A., Italy

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE	
WO 9632380	A1	19961017	WO 1996-EP1165 19960314	
W: JP, US				
RW: AT, BE,	CH, DE	, DK, ES,	FI, FR, GB, GR, IE, IT, LU, MC, NL, 1	PT, SE
EP 764152	A1	19970326	EP 1996-907500 19960314	
R: DE, ES,	FR, GB	, IT, SE		
JP_10501821	T2	19980217	JP 1996-530667 19960314	
US 5849710	A	19981215	US 1996-750208 19961204	
PRIORITY APPLN. INFO.	.:		GB 1995-7298 19950407	
			WO 1996-EP1165 19960314	

OTHER SOURCE(S):

MARPAT 126:18783

GΙ

Indol-3-ylmethylene-2-oxindole derivs. I and their pharmaceutically AΒ acceptable salts are disclosed [wherein 1 or 2 of R, R1, R2, and R3 = X(CH2)mNH2, X(CH2)mNR4R5, X(CH2)mNHR6, NHC(:NH)NH2, NHC(:NH)NR4R5, NHC(:NH)NHR6, N:CHNH2, N:CHNR4R5, N:CHNHR6, X(CH2)mCOR7, CORa, COR8, YCOY'R9, NHR6, NHR10 group; remaining groups within R and R1-R3 = H, halo,

II

amino, OH, alkyl, alkoxy, CO2H, alkoxycarbonyl, alkanoyloxy, cyano, NR4R5; X = O, S, NH; m = 1-4; 1 of R4 and R5 = H or alkyl, and other = alkyl; or NR4R5 forms satd. monoheterocycle; R6 = alkanoyl, 1- to 3-residue (un)substituted peptidyl; R7 = OH, amino, alkoxy, NR4R5; Ra = amino terminus of 1- to 3-unit peptidyl; R8 = alkoxy, phenylalkoxy, (CH2)nNH2, (CH2)nNR4R5, (CH2)nNHR6; n = 1-2; Y, Y' = NH, O; R9 = Ph, alkyl, phenylalkyl; R10 = mono-, di- or trihydroxyalkyl]. I have tyrosine kinase inhibiting activity, and are useful as antiproliferative, antimetastatic, anticancer, antiatheromatous, anti-Alzheimer, and immunomodulating agents. For example, 2-indolinone reacted with BrCH2COBr and AlCl3 to give the 5-(2-bromoacetyl) deriv., which underwent amination with piperidine and then condensation with indole-3-carboxaldehyde, to give title compd. II (FCE 28484). In tests for inhibition of p45 v-abl kinase and K562 leukemia cells in vitro, II had IC50 of 0.78 and 4.82 .mu.M, resp.

IT 184020-79-9P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

RN 184020-79-9 CAPLUS

CN Methanimidamide, N'-[2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

L65 ANSWER 42 OF 70 USPATFULL

ACCESSION NUMBER: 2002:67225 USPATFULL

TITLE: Prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone

derivatives

INVENTOR(S): Moon, Malcolm Wilson, Kalamazoo, MI, UNITED STATES

Morozowich, Walter, Kalamazoo, MI, UNITED STATES

Gao, Ping, Portage, MI, UNITED STATES

Koenig, Marcel, Burlingame, CA, UNITED STATES

NUMBER DATE

PRIORITY INFORMATION: US 2000-207000P 20000524 (60) US 2000-225045P 20000811 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Beth A. Burrous, FOLEY & LARDNER, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: 56 EXEMPLARY CLAIM: 1 LINE COUNT: 4248

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to prodrugs of certain

3-(pyrrol-2-yl-methylidene)-2-indolinone derivatives that modulate the

09/716332

activity of protein kinases ("PKs"). Pharmaceutical compositions comprising these compounds, methods of treating diseases related to abnormal PK activity utilizing pharmaceutical compositions comprising these compounds and methods of preparing them are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

375387-20-5P 375798-46-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375387-20-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(1-pyrrolidinylmethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

375798-46-2 USPATFULL RN

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, dihydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

• 2 HC1

326914-13-0P 375798-54-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 326914-13-0 USPATFULL

1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-CN dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Page 268

RN 375798-54-2 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(hydroxymethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 375798-45-1P 375798-47-3P 375798-48-4P

375798-49-5P 375798-50-8P 375798-51-9P 375798-52-0P 375798-53-1P 375798-55-3P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375798-45-1 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-47-3 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-hydroxy-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 375798-48-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-methyl-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-49-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[[2-(methoxymethyl)-1-pyrrolidinyl]methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-50-8 USPATFULL

CN L-Proline, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 375798-51-9 USPATFULL

CN 2H-Indol-2-one, 1-[(3,5-dimethyl-1-piperazinyl)methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-52-0 USPATFULL

CN

2H-Indol-2-one, 1-[[bis(2-methoxyethyl)amino]methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-53-1 USPATFULL

CN Pyridinium, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]-, chloride (9CI) (CA INDEX NAME)

● c1-

RN 375798-55-3 USPATFULL

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-yrole-3-carboxamide)]fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H. & O & Me \\ \hline N & O & Me \\ \hline Z & Me & OH \\ \hline N & H & OH \\ \end{array}$$

L65 ANSWER 43 OF 70 USPATFULL

ACCESSION NUMBER:

TITLE:

2002:61304 USPATFULL

1-(pyrrlolidin-1-ylmethyl)-3-(pyrrol-2-ylmethylidene)-2indolinone derivatives

INVENTOR(S):

Moon, Malcolm Wilson, Kalamazoo, MI, UNITED STATES Morozowich, Walter, Kalamazoo, MI, UNITED STATES

Gao, Ping, Portage, MI, UNITED STATES

NUMBER KIND DATE PATENT INFORMATION: US 2002035140 Α1 20020321 APPLICATION INFO.: US 2001-863905 A1 20010524 (9)

NUMBER DATE

> 20000524 (60) US 2000-207000P US 2000-225045P 20000811 (60)

DOCUMENT TYPE: Utility

APPLICATION

FILE SEGMENT: LEGAL REPRESENTATIVE:

Beth A. Burrous, FOLEY & LARDNER, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: 21 EXEMPLARY CLAIM: LINE COUNT:

PRIORITY INFORMATION:

2979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to 1-pyrrolidin-1-ylmethyl-3-(pyrrol-2ylmethylidene)-2-indolinone derivatives that modulate the activity of **protein kinases** ("PKs"). Pharmaceutical compositions comprising these compounds, methods of treating diseases related to abnormal PK activity utilizing pharmaceutical compositions comprising these compounds and methods of preparing them are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 375387-20-5P 375798-46-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375387-20-5 USPATFULL

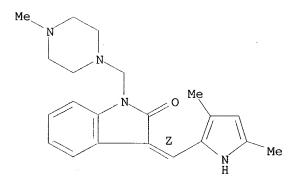
CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(1-pyrrolidinylmethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-46-2 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1[(4-methyl-1-piperazinyl)methyl]-, dihydrochloride, (3Z)- (9CI) (CA
INDEX NAME)

Double bond geometry as shown.



●2 HCl

IT 326914-13-0P 375798-54-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 326914-13-0 USPATFULL

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 375798-54-2 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(hydroxymethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 375798-45-1P 375798-47-3P 375798-48-4P

375798-49-5P 375798-50-8P 375798-51-9P

375798-52-0P 375798-53-1P 375798-55-3P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375798-45-1 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-47-3 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-hydroxy-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 375798-48-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-methyl-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-49-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[[2-(methoxymethyl)-1-pyrrolidinyl]methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-50-8 USPATFULL

CN L-Proline, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 375798-51-9 USPATFULL

CN 2H-Indol-2-one, 1-[(3,5-dimethyl-1-piperazinyl)methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-52-0 USPATFULL

CN 2H-Indol-2-one, 1-[[bis(2-methoxyethyl)amino]methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-53-1 USPATFULL

CN Pyridinium, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]-, chloride (9CI) (CA INDEX NAME)

● C1 -

RN 375798-55-3 USPATFULL

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L65 ANSWER 44 OF 70 USPATFULL

ACCESSION NUMBER:

2002:55041 USPATFULL

TITLE:

Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-

indolinone derivatives

INVENTOR(S):

Moon, Malcolm Wilson, Kalamazoo, MI, UNITED STATES Morozowich, Walter, Kalamazoo, MI, UNITED STATES

Gao, Ping, Portage, MI, UNITED STATES
Tang, Peng Cho, Moraga, CA, UNITED STATES

		NUMBER	KIND	DATE	
PATENT INFORMATION:	US	2002032204	A1	20020314	
APPLICATION INFO.:	US	2001-863804	A1	20010524	(9)

NUMBER DATE

US 2000-207000P 20000524 (60) US 2000-225045P 20000811 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

PRIORITY INFORMATION:

Beth A. Burrous, FOLEY & LARDNER, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

36

LINE COUNT:

1 3353

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention is directed to Mannich base prodrugs of certain 3-(pyrrol-2-ylmethylidene)-2-indolinone derivatives that modulate the activity of protein kinases ("PKs"). Pharmaceutical compositions comprising these compounds, methods of treating diseases related to abnormal PK activity utilizing pharmaceutical compositions comprising these compounds and methods of preparing them are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 375387-20-5P 375798-46-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375387-20-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(1-pyrrolidinylmethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-46-2 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, dihydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●2 HCl

IT 326914-13-0P 375798-54-2P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 326914-13-0 USPATFULL

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-54-2 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-(hydroxymethyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

IT 375798-45-1P 375798-47-3P 375798-48-4P

375798-49-5P 375798-50-8P 375798-51-9P

375798-52-0P 375798-53-1P 375798-55-3P

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375798-45-1 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(4-methyl-1-piperazinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-47-3 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-hydroxy-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 375798-48-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[(2-methyl-1-pyrrolidinyl)methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-49-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-1-[[2-(methoxymethyl)-1-pyrrolidinyl]methyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-50-8 USPATFULL

CN L-Proline, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 375798-51-9 USPATFULL

CN 2H-Indol-2-one, 1-[(3,5-dimethyl-1-piperazinyl)methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-52-0 USPATFULL

CN 2H-Indol-2-one, 1-[[bis(2-methoxyethyl)amino]methyl]-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 375798-53-1 USPATFULL

CN Pyridinium, 1-[[(3Z)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]-, chloride (9CI) (CA INDEX NAME)

● c1-

RN 375798-55-3 USPATFULL

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L65 ANSWER 45 OF 70 USPATFULL

ACCESSION NUMBER: 2002:48648 USPATFULL

TITLE: 2-indolinone derivatives as modulators of

protein kinase activity

INVENTOR(S): Tang, Peng Cho, Moraga, CA, UNITED STATES
Sun, Li, Foster City, CA, UNITED STATES

Sun, Li, Foster City, CA, UNITED STATES McMahon, Gerald, Kenwood, CA, UNITED STATES

Harris, G. Davis, JR., San Francisco, CA, UNITED STATES

(9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-293518, filed on 15

Apr 1999, GRANTED, Pat. No. US 6316635

NUMBER DATE

PRIORITY INFORMATION: US 1998-82056P 19980416 (60) DOCUMENT TYPE: Utility

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Beth A. Burrous, FOLEY & LARDNER, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: 30 EXEMPLARY CLAIM: 1 LINE COUNT: 2811 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel imidazoly 2-indolinones and physiologically acceptable salts and prodrugs thereof which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5P, SU 5408 186610-93-5P, SU 5404
186610-94-6P, SU 5406 186611-14-3P, SU 5402
186611-15-4P, SU 5403 186611-16-5P, SU 5405
186611-17-6P, SU 5407 186611-29-0P, SU 5453
186611-30-3P, SU 5454 186611-31-4P, SU 5455
186611-32-5P, SU 5456 186611-33-6P, SU 5459
186611-34-7P, SU 5460 186611-37-0P, SU 5463
186611-39-2P, SU 5465 186611-48-3P, SU 5477
186611-49-4P, SU 5478 186611-50-7P, SU 5479
186611-54-1P, SU 5613 186611-56-3P, SU 5614
186611-66-5P, SU 5625 186611-67-6P, SU 5626
204005-46-9P, SU 5416

(prepn. of indolinones capable of modulating tyrosine kinase signal transduction)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm CH}_{
m CH_2-CH_2-CO_2H}$

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

.CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-32-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & & CH_2 - C - OMe \\ \hline & & & & & \\ & & & & & \\ & & & & & \\ \end{array}$$

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-49-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 USPATFULL

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & Me & C-Me \\ & || \\ & CH_2 \\ \end{array}$$

RN 186611-54-1 USPATFULL

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-56-3 USPATFULL

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-66-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 H
 O
 CH
 H
 N
 Me

RN 186611-67-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline O_2N & CH & Me \\ \hline \end{array}$$

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 46 OF 70 USPATFULL

ACCESSION NUMBER:

2002:43684 USPATFULL

TITLE:

Novel 3-(substituted) -2- indolinones compounds and use

thereof as inhibitors of protein

kinase activity

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, UNITED STATES Sun, Li, Foster City, CA, UNITED STATES McMahon, Gerald, Kenwood, CA, UNITED STATES

NUMBER KIND DATE PATENT INFORMATION: US 2002026053 Α1 20020228 APPLICATION INFO.: US 2001-916331 A1 20010730 (9)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-516948, filed on 1 Mar 2000, ABANDONED Division of Ser. No. US 1998-161046,

filed on 25 Sep 1998, GRANTED, Pat. No. US 6133305

DATE NUMBER

PRIORITY INFORMATION:

US 1997-60194P 19970926 (60)

DOCUMENT TYPE: FILE SEGMENT:

Utility APPLICATION

LEGAL REPRESENTATIVE:

Beth A. Burrous, FOLEY & LARDNER, Washington Harbour,

3000 K Street N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

LINE COUNT:

1 5540

20

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-(substituted)-2-indolinones compounds and physiologically acceptable salts and prodrugs thereof which modulate the activity of protein kinases and

therefore are expected to be useful in the prevention and treatment of protein kinase related disorders such as

cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5 215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

15966-93-5 USPATFULL RN

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ Br & & \\ & & \\ Br & & \\ Me & & \\ Et & & \\ \end{array}$$

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 Me

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

215543-97-8 USPATFULL RN

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 47 OF 70 USPATFULL

ACCESSION NUMBER:

INVENTOR(S):

2002:37906 USPATFULL

TITLE:

Indolinone combinatorial libraries and related products

and methods for the treatment of disease Tang, Peng Cho, Moraga, CA, UNITED STATES

Sun, LI, Foster City, CA, UNITED STATES

McMahon, Gerald, San Francisco, CA, UNITED STATES Hirth, Klaus Peter, San Francisco, CA, UNITED STATES Shawver, Laura Kay, San Francisco, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002022626	A1	20020221	
APPLICATION INFO.:	US 2000-617529	A1	20000713	(9)
RELATED APPLN. INFO.:	Division of Ser.	No. US	1997-9153	66, filed on 20 Aug
	1997, GRANTED, P	at. No.	US 614710	6
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	BETH A BURROUS,	FOLEY &	LARDNER,	WASHINGTON HARBOUR,
	30000 K STREET,	N.W., W	ASHINGTON,	DC, 20007-5109
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	42 Drawing Page (s)		

LINE COUNT: 7888

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating, regulating and/or inhibiting protein kinase signal transduction. Such compounds are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis and restenosis and metabolic diseases such as diabetes. The present invention features indolinone compounds that potently inhibit **protein kinases** and related products and methods. Inhibitors specific to the FLK **protein kinase** can be obtained by adding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone, in particular at the 1' position of the indole ring. Indolinone compounds that specifically inhibit the FLK and platelet derived growth factor **protein kinases** can harbor a tetrahydroindole or cyclopentano-b-pyrrol moiety. Indolinone compounds that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate **protein kinases**. This invention also features novel hydrosoluble indolinone compounds that are tyrosine kinase inhibitors and related products and methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT: IT **203988-42-5P**, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone 203988-54-9P, 3-[(3,4-Dibromo-2methylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone 203988-64-1P 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2indolinone 203988-74-3P, 3-[(3,4-Dibromo-2-methylpyrrol-5y1)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone **203988-84-5P**, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone **203988-94-7P**, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl) -2-indolinone 203989-04-2P, $3-[(3,4-\texttt{Dibromo-2-methylpyrrol-5-yl})\,\texttt{methylidenyl}] - 5-(2-\texttt{chloroethyl}) - 2-(2-\texttt{chloroethyl}) - 2-(2-\texttt$ indolinone 203989-05-3P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5,7-dibromo-2-indolinone **203989-08-6P**, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5,7-dibromo-2indolinone 203989-14-4P, 3-[[2,4-Dimethyl-3- $(\verb"ethoxycarbonyl") \verb"pyrrol-5-yl"] \verb"methylidenyl"] - 5-iodo-2-indolinone$ 203989-17-7P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-iodo-2-indolinone **203989-24-6P**, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203989-27-9P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-bromo-4-methyl-2indolinone 203989-35-9P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-[(methylamino)sulfonyl]-2indolinone 203989-40-6P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone **203989-52-0P**, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2indolinone 203989-56-4P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2indolinone 203989-65-5P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-(morpholinosulfonyl)-2indolinone 203989-68-8P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5yl]methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203989-75-7P , 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-(2chloroethyl)-2-indolinone 203989-78-0P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203989-88-2P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2indolinone 203989-98-4P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5v1)methylidenyl]-5-iodo-2-indolinone 203990-08-3P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2indolinone 203990-18-5P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone **203990-28-7P**, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-

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[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203990-38-9P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203990-48-1P,
3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-
indolinone 203991-62-2P, 3-[(2,4-Dimethylpyrrol-5-
yl)methylidenyl]-5,7-dibromo-2-indolinone 203991-72-4P,
3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone
203991-82-6P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-bromo-4-
methyl-2-indolinone 203991-92-8P, 3-[(2,4-Dimethylpyrrol-5-
yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203992-02-3P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-12-5P
, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203992-22-7P, 3-[(2,4-Dimethylpyrrol-5-
yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone 203994-35-8P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5,7-dibromo-2-indolinone 203994-53-0P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203994-72-3P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203994-91-6P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203995-11-3P, 3-[[2-Chloro-4-(methoxycarbonyl)-3-
[(methoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-[[[4-
(\verb|trifluoromethy|) | pheny|] | amino| sulfony|] - 2 - indolinone | \textbf{203995-26-0P}| | constant |
   3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203995-36-2P
, 3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203995-39-5P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5,7-dibromo-2-indolinone 203995-48-6P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203995-57-7P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203995-66-8P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203995-75-9P, 3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-
methylpyrrol-5-yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulf
onyl]-2-indolinone 203995-84-0P, 3-[[2-(Ethoxycarbonyl)-4-
(methoxycarbonyl)-3-methylpyrrol-5-yl]methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203995-93-1P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203996-03-6P,
3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone
203996-13-8P, 3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-iodo-2-
indolinone 203996-23-0P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203996-33-2P,
3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203996-43-4P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 203996-53-6P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203996-63-8P
   3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
204003-90-7P 204003-91-8P 204003-96-3P
204003-97-4P 204004-29-5P 204004-86-4P
204004-92-2P 204004-94-4P 204005-03-8P
204005-21-0P 204005-38-9P 204005-39-0P
204005-46-9P 204005-54-9P 204005-56-1P
204005-58-3P 204005-59-4P
   (prepn. and testing of indolinone combinatorial library as protein
   kinase inhibitors)
```

RN 203988-42-5 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203988-54-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203988-64-1 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203988-74-3 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203988-84-5 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203988-94-7 USPATFULL

CN Morpholine, 4-[[3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & H & O & H \\ \hline O & S & CH & N & Me \\ \hline O & Br & Br & Br \\ \end{array}$$

RN 203989-04-2 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203989-05-3 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-08-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-14-4 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-17-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-24-6 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-27-9 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-

indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-,
ethyl ester (9CI) (CA INDEX NAME)

RN 203989-35-9 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-40-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-52-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-56-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-65-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-68-8 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-75-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline ClCH_2-CH_2 & & H & Me \\ \hline \\ Me & C-OEt \\ || & O \\ \end{array}$$

RN 203989-78-0 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O & O \\ \hline CH & N & C-OEt \\ \hline CH & CH_2-CH_2-CH_2-C-OEt \\ \hline \end{array}$$

RN 203989-88-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 203989-98-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203990-08-3 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203990-18-5 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN, 203990-28-7 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203990-38-9 USPATFULL

CN Morpholine, 4-[[3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & H & M \\ \hline O & N & S \\ \hline O & O & Me \\ \hline \end{array}$$

RN 203990-48-1 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203991-62-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203991-72-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203991-82-6 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203991-92-8 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203992-02-3 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203992-12-5 USPATFULL

CN Morpholine, 4-[[3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203992-22-7 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 H
 N
 CH
 H
 N
 Me

RN 203994-35-8 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

09/716332

RN 203994-53-0 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline I & CH & CH & C1 \\ \hline MeO-C & CH_2-C-OMe \\ O & \\ \end{array}$$

RN 203994-72-3 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-chloro-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203994-91-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-11-3 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-26-0 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-36-2 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-39-5 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-48-6 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-57-7 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & O \\ & H & C - OEt \\ & Me & MeO-C & Me \\ & O & & \end{array}$$

RN 203995-66-8 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-75-9 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$F_3C$$
 $NH-S$
 $MeO-C$
 Me
 $NH-S$
 N

RN 203995-84-0 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

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RN 203995-93-1 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & O \\ & H & C - OEt \\ \hline & CH & Me \\ & O & Me \\ & O & \\ \end{array}$$

RN 203996-03-6 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203996-13-8 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203996-23-0 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ \hline & N & O \\ \hline & CH & N \\ \hline & Et \\ \end{array}$$

RN 203996-33-2 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203996-43-4 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203996-53-6 USPATFULL

CN Morpholine, 4-[[3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203996-63-8 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204003-90-7 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-91-8 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-96-3 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)

RN 204003-97-4 USPATFULL

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ HO_2C-CH_2-CH_2 & CH & Me \end{array}$$

RN 204004-29-5 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline H_2N & CH & Br & Br \end{array}$$

RN 204004-86-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-amino-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

Jones

$$H_2N$$
 H_2N
 H_2N

RN 204004-92-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

C1
$$\stackrel{\text{H}}{\sim}$$
 $\stackrel{\text{O}}{\sim}$ $\stackrel{\text{H}}{\sim}$ $\stackrel{\text{H}}{\sim}$

RN 204004-94-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 204005-03-8 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & \\ \hline & CH & \\ \hline & Me & CH_2-CH_2-C-OMe \end{array}$$

RN 204005-21-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,2,4-trimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 204005-38-9 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2N}$$
 H_{2N}
 H

RN 204005-39-0 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-54-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 204005-56-1 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-58-3 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-59-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

L65 ANSWER 48 OF 70 USPATFULL

ACCESSION NUMBER:

INVENTOR(S):

2001:237974 USPATFULL

TITLE:

3-(Cycloalkanoheteroarylidenyl)-2-Indolinone

Protein Tyrosine Kinase Inhibitors

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

NUMBER KIND DATE

Page 315

PATENT INFORMATION: US 2001056094 A1 20011227

US 6350754 B2 20020226

APPLICATION INFO.: US 2000-482198 A1 20000112 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-99721, filed on 19 Jun

1998, GRANTED, Pat. No. US 6051593

NUMBER DATE

PRIORITY INFORMATION: US 1997-50413P 19970620 (60)

US 1997-59544P 19970919 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BETH A. BURROUS, FOLEY & LARDNER, WASHINGTON HARBOUR,

3000 K STREET, N.W., STE: 500, WASHINGTON, DC,

20007-5109

NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 3325

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-(cycloalkano-heteroarylidenyl)-

2-indolinone compounds and physiologically acceptable salts and prodrugs thereof which are expected to modulate the activity of protein

tyrosine kinases and therefore to be useful in the prevention

and treatment of protein tyrosine kinase related

cellular disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ CH \\ \end{array}$$

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 49 OF 70 USPATFULL

ACCESSION NUMBER:

2001:171157 USPATFULL

TITLE: 3-(4'-bromobenzylindenyl)-2-indolinone and analogues

thereof for the treatment of disease

INVENTOR(S): Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

NUMBER KIND DATE ______ _____ PATENT INFORMATION: US 2001027207 A1 20011004 APPLICATION INFO.: US 2001-765619 Α1 20010122 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-212494, filed on 15

Dec 1998, GRANTED, Pat. No. US 6225335

Continuation-in-part of Ser. No. US 1995-485323, filed

on 7 Jun 1995, GRANTED, Pat. No. US 5880141

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

Beth A. Burrous, FOLEY & LARDNER, Washington Harbour, LEGAL REPRESENTATIVE:

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5109

NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1 LINE COUNT: 3391

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

15966-93-5P, SU 5408 186610-93-5P, SU 5404 186610-94-6P, SU 5406 186611-14-3P, SU 5402 186611-15-4P, SU 5403 186611-16-5P, SU 5405 **186611-17-6P**, SU 5407 **186611-29-0P**, SU 5453 **186611-30-3P**, SU 5454 **186611-31-4P**, SU 5455

> 186611-32-5P, SU 5456 186611-33-6P, SU 5459 **186611-34-7P**, SU 5460 **186611-37-0P**, SU 5463

> **186611-39-2P**, SU 5465 **186611-48-3P**, SU 5477

186611-49-4P, SU 5478 **186611-50-7P**, SU 5479 186611-54-1P, SU 5613 186611-56-3P, SU 5614

186611-66-5P, SU 5625 **186611-67-6P**, SU 5626

204005-46-9P, SU 5416

(prepn. of indolinones capable of modulating tyrosine kinase signal transduction)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & CH & \\ \hline & CH_2-CH_2-CO_2H \\ \end{array}$$

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-32-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & CH_2-C-OMe \\ \hline & O & CH_2-C-OMe \\ \hline &$$

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-49-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 USPATFULL

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-54-1 USPATFULL

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-56-3 USPATFULL

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-66-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

186611-67-6 USPATFULL RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-CN nitro- (9CI) (CA INDEX NAME)

204005-46-9 USPATFULL RN

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-CN (9CI) (CA INDEX NAME)

L65 ANSWER 50 OF 70 USPATFULL

ACCESSION NUMBER:

TITLE:

2001:105414 USPATFULL Novel 3-(substituted)-2=indolinones compounds and use

thereof as inhibitors of protein /

kinase activity

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

NUMBER KIND DATE PATENT INFORMATION: US 2001007033 A1 20010705 US 2000-516948 A1 20000301 (9)- ... APPLICATION INFO.: Division of Ser. No. US 1998-161046, filed on 25 Sep RELATED APPLN. INFO.: 1998, PENDING

NUMBER DATE

PRIORITY INFORMATION:

US 1997-60194P 19970926 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

BETH A BURROUS, FOLEY & LARDNER WASHINGTON HARBOUR,

3000 K STREET, N.W., WASHINGTON, DC, 20007-5109

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

LINE COUNT:

4626 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-(substituted)-2-indolinones compounds and physiologically acceptable salts and prodrugs thereof which modulate the activity of protein kinases and therefore are expected to e useful in the prevention and treatment of protein kinase related disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

15966-93-5 USPATFULL RN

CN 1H-Pyrrole-3-carboxylic acid, 5-{(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (CA INDEX NAME)

186611-31-4 USPATFULL RN

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-

Page 330

dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ Br & & \\ & & \\ Me & & \\ Et & & \\ \end{array}$$

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 Me

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & N & O & \\ \hline & CH & N & \\ \hline & Me & CH_2-CH_2-C-OEt \\ \end{array}$$

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 51 OF 70 USPATFULL

ACCESSION NUMBER:

2001:202612 USPATFULL

TITLE:

Bicyclic protein kinase inhibitors

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., South San Francisco, CA, United States

(U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION: US 1997-45838P 19970507 (60) US 1997-59677P 19970919 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Raymond, Richard L.
ASSISTANT EXAMINER: Truong, Tamthom N.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 10

NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1 LINE COUNT: 3756

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-idene-2-indolinone compounds and physiologically acceptable salts thereof which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN 15966-93-5 USPATFULL

CN

1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 Me

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{N}$$
 $\stackrel{O}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{O}{\sim}$ $\stackrel{H}{\sim}$ $\stackrel{H}{\sim}$

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 52 OF 70 USPATFULL

ACCESSION NUMBER:

2001:197055 USPATFULL

TITLE:

Bioavailability of 3-heteroarylidenyl-2-indolinones

active as protein tyrosine kinase

inhibitors

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION: US	6313158	B1	20011106	
APPLICATION INFO.: US	1998-100854		19980619	(9)

NUMBER DATE

PRIORITY INFORMATION:

US 1997-50412P 19970620 (60) US 1997-59336P 19970919 (60)

Utility

DOCUMENT TYPE: FILE SEGMENT:

GRANTED

PRIMARY EXAMINER:

Shah, Mukund J. McKenzie, Thomas C

ASSISTANT EXAMINER: LEGAL REPRESENTATIVE:

Foley & Lardner

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

21

3273

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AΒ The present invention relates to novel 3-heteroarylidenyl-2-indolinone compounds and physiologically acceptable salts and prodrugs thereof which have improved hydrosolubility and which are expected to modulate the activity of protein tyrosine kinases and

therefore should be useful in the prevention and treatment of

protein tyrosine kinase related cellular disorders

such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

15966-93-5 USPATFULL RN

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & CH_2-C-OMe \\ \hline & O & CH_2-C-OMe \\ \end{array}$$

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ Br & & \\ Me & & \\ Me & & \\ \end{array}$$

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & \\ Br & & \\ & & \\ Me & & \\ Et & & \\ \end{array}$$

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\underset{N}{\bigvee}}$$
 $\stackrel{O}{\underset{N}{\bigvee}}$ $\stackrel{H}{\underset{N}{\bigvee}}$ $\stackrel{O}{\underset{N}{\bigvee}}$ $\stackrel{O}{\underset{N}{\bigvee}}$ $\stackrel{O}{\underset{N}{\bigvee}}$ $\stackrel{O}{\underset{N}{\bigvee}}$

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

215543-97-8 USPATFULL RN

1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 53 OF 70 USPATFULL

2001:185487 USPATFULL ACCESSION NUMBER:

TITLE: 4-aryloxindoles

INVENTOR(S): Corbett, Wendy Lea, Randolph, NJ, United States

Luk, Kin-Chun, North Caldwell, NJ, United States Mahaney, Paige E., Montclair, NJ, United States

PATENT ASSIGNEE(S): Hoffman-La Roche Inc., Nutley, NJ, United States (U.S.

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6307056	В1	20011023	
APPLICATION INFO :	IIS 1999-464466		19991215	191

NUMBER DATE

US 1998-112590P 19981217 (60) PRIORITY INFORMATION:

US 1999-149028P 19990816 (60) DOCUMENT TYPE:

Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Higel, Floyd D.

LEGAL REPRESENTATIVE: Johnston, George W., Rocha-Tramaloni, Patricia S.

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1 LINE COUNT: 3094

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are 4-aryloxindoles that inhibit or modulate protein

kinases, in particular JNK protein kinases.

These compounds and their pharmaceutically acceptable salts, and prodrugs of said compounds, are useful as anti-inflammatory agents, particularly useful in the treatment of rheumatoid arthritis.

Also disclosed are pharmaceutical compositions containing the foregoing compounds, as well as methods for the treatment and/or control of

inflammation, particularly in the treatment or control of rheumatoid arthritis, using said compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 276251-67-3P

(prepn. of 4-aryl-3-(azolylmethylidene)-2-oxindoles as inhibitors of JNK protein kinases)

RN 276251-67-3 USPATFULL

CN 2H-Indol-2-one, 5-fluoro-1,3-dihydro-4-(4-hydroxyphenyl)-3-[(3-methyl-1Hpyrrol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L65 ANSWER 54 OF 70 USPATFULL

ACCESSION NUMBER:

2001:179279 USPATFULL

TITLE: INVENTOR(S):

4-alkenyl-and 4-alkynyloxindoles Chen, Yi, Nutley, NJ, United States

Dermatakis, Apostolos, North Brunswick, NJ, United

States

Liu, Jin-Jun, Warren, NJ, United States

Luk, Kin-Chun, North Caldwell, NJ, United States

PATENT ASSIGNEE(S):

Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S.

corporation)

	•	NUMBER	KIND	DATE	
PATENT INFORMATION:	US	6303793	B1	20011016	
APPLICATION INFO.:	US	2000-566054		20000505	(9)
DELATED ADDING THEO .	Dist	ision of Cor	Mo IIC	1000-1615	02

Division of Ser. No. US 1999-464502, filed on 15 Dec

1999, now patented, Pat. No. US 6130239

	NUMBER	DATE			
PRIORITY INFORMATION:	US 1998-112591P	19981217	(60)		
intentil intentilion.	US 1999-149073P	19990816			
DOCUMENT TYPE:	Utility				
FILE SEGMENT:	GRANTED				
PRIMARY EXAMINER:	Aulakh, C. S.				
LEGAL REPRESENTATIVE:	Johnston, George	W., Rocha-T	ramaloni,	Patricia	s.
NUMBER OF CLAIMS:	3				
EXEMPLARY CLAIM:	1				
LINE COUNT:	4113				
CAC TUDDUTUG TO AUATIADID DOD MUTG DAMBUM					

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel 4-alkenyl- and 4-alkynyl oxindoles having the formula ##STR1##

09/716332

and the pharmaceutically acceptable salts thereof, wherein R.sup.1, R.sup.2, R.sup.3, a, b, and X are as defined herein. These compounds inhibit cyclin-dependent kinases (CDKs), in particular CDK2. These compounds and their pharmaceutically acceptable salts, and prodrugs of said compounds, are anti-proliferative agents useful in the treatment or control of cell proliferative disorders, in particular cancer, more particularly, the treatment or control of breast and colon tumors. Also disclosed are pharmaceutical compositions containing the compounds of formula I and II as well as intermediates useful in the preparation of the compounds of formula I and II.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 275387-68-3P, (Z)-3-[(4-Acetyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-fluoro-4-iodo-2H-indol-2-one 275387-99-0P

275388-01-7P 275388-18-6P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275387-68-3 USPATFULL

CN

2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-iodo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-99-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-01-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-18-6 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

$$\begin{array}{c|c} & H & O & Me \\ \hline & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 275387-73-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-74-1 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275387-77-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 275387-78-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

HC1

RN 275388-00-6 USPATFULL

CN

2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

$$\begin{array}{c} H \\ N \\ C \\ \end{array}$$

● HCl

RN 275388-02-8 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

● HCl

RN 275388-03-9 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,3-dihydro-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & AC \\ \hline & & & \\ EtNH & C & & H \end{array}$$

HC1

RN 275388-04-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(4-hydroxy-4-piperidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

HC1

RN 275388-10-8 USPATFULL

CN

1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & Me \\ \hline & V & \\ \hline & & \\ EtNH & C \\ \hline & C \\ \hline \end{array}$$

HC1

RN 275388-19-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

$$\begin{array}{c|c} H & O & Me \\ \hline C & \hline C & \\ HN & S & \\ \end{array}$$

HCl

RN 275388-31-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-[(2-hydroxypropyl)amino]-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & Ac \\ \hline OH & H & F & \\ Me & C = C & H \end{array}$$

● HCl

RN 275388-32-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-(ethylamino)-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-33-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(2R)-3-(ethylamino)-2-methyl-2H-pyran-6-yl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 275388-34-6 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-km]

amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-35-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3S,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

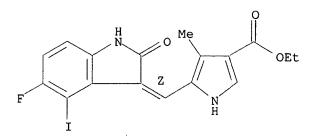
Absolute stereochemistry. Double bond geometry as shown.

IT 275388-09-5P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275388-09-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(5-fluoro-1,2-dihydro-4-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



L65 ANSWER 55 OF 70 USPATFULL

ACCESSION NUMBER: 2001:98105 USPATFULL

4-alkenyl-and 4-alkynyloxindoles TITLE: INVENTOR(S): Chen, Yi, Nutley, NJ, United States

Dermatakis, Apostolos, North Brunswick, NJ, United

States

Luk, Kin-Chun, North Caldwell, NJ, United States

PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S.

corporation)

KIND DATE NUMBER US 6252086 PATENT INFORMATION: В1 20010626 US 2000-549864

APPLICATION INFO.: 20000414 (9) Division of Ser. No. US 1999-464502, filed on 15 Dec RELATED APPLN. INFO.:

1999, now patented, Pat. No. US 6130239, issued on 10

Oct 2000

NUMBER DATE ______

PRIORITY INFORMATION:

US 1998-112591P 19981217 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Higel, Floyd D.

Johnston, George W., Rocha-Tramaloni, Patricia S. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: LINE COUNT: 4328

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are novel 4-alkenyl- and 4-alkynyl oxindoles having the AB

formula ##STR1##

and the pharmaceutically acceptable salts thereof. These compounds inhibit cyclin-dependent kinases (CDKs), in particular CDK2. These compounds and their pharmaceutically acceptable salts, and prodrugs of said compounds, are anti-proliferative agents useful in the treatment or control of cell proliferative disorders, in particular cancer, more particularly, the treatment or control of breast and colon tumors. Also disclosed are pharmaceutical compositions containing the compounds of formula I and II as well as intermediates useful in the preparation of the compounds of formula I and II.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

275387-68-3P, (Z)-3-[(4-Acetyl-1H-pyrrol-2-yl)methylene]-1,3-

dihydro-5-fluoro-4-iodo-2H-indol-2-one 275387-99-0P

275388-01-7P 275388-18-6P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole

anti-proliferatives and analogs by reaction of alkynes with the

corresponding 4-halo-2-oxoindoles)

RN 275387-68-3 USPATFULL CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-iodo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-99-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-01-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-18-6 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

N 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(tetrahydro-4-hydroxy-2H-pyran-4-yl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-73-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 275387-74-1 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275387-77-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-78-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

● HCl

RN 275388-00-6 USPATFULL CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

● HCl

RN 275388-02-8 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HCl

RN 275388-03-9 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,3-dihydro-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & H & O & AC \\ \hline & Z & & N \\ \hline & E t N H & C \end{array}$$

● HCl

RN 275388-04-0 USPATFULL

CN

2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(4-hydroxy-4-piperidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

● HCl

RN 275388-10-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & H & O & Me \\ \hline & N & O & Me \\ \hline & EtNH & C \end{array}$$

● HCl

RN 275388-19-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

● HCl

RN 275388-31-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-[(2-hydroxypropyl)amino]-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275388-32-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-(ethylamino)-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-33-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(2R)-3-(ethylamino)-2-methyl-2H-pyran-6-yl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-34-6 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-35-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3S,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

IT 275388-09-5P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275388-09-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(5-fluoro-1,2-dihydro-4-iodo-2-oxo-3Hindol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L65 ANSWER 56 OF 70 USPATFULL

2001:75421 USPATFULL ACCESSION NUMBER:

TITLE: Methods of preventing and treating neurological

disorders with compounds that modulate the function of

the C-RET receptor protein tyrosine

INVENTOR(S): Clary, Douglas, San Francisco, CA, United States

PATENT ASSIGNEE(S): Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

NUMBER DATE KIND PATENT INFORMATION: US 6235769 В1 20010522 US 1998-109883 19980702 APPLICATION INFO.: (9)

NUMBER DATE

PRIORITY INFORMATION: US 1997-51715P 19970703 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

Criares, Theodore J.

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Foley & Lardner

NUMBER OF CLAIMS: 14 EXEMPLARY CLAIM: 1 2371 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates in part to a method of preventing or treating an abnormal condition caused by an aberration in the function of the C-RET receptor, and specifically to the treatment and prevention of neurodegenerative disorders by administering a pharmaceutical composition that modulates the function of the C-RET receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 204003-90-7 204003-91-8 204003-96-3

204003-97-4

(study and treatment of diseases related to specific cellular functions of receptor protein tyrosine kinases, and screening method)

RN 204003-90-7 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-91-8 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-96-3 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C$$
 HO_2C
 HO_2C
 HO_2C
 HO_2C
 HO_2C

RN 204003-97-4 USPATFULL

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$
 $HO_2C-CH_2-CH_2$

L65 ANSWER 57 OF 70 USPATFULL

ACCESSION NUMBER: 2001:63712 USPATFULL

TITLE: 3-(4'-bromobenzylindenyl)-2-indolinone and analogues

thereof for the treatment of disease

INVENTOR(S): Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S): Sugen, Inc., Red City, CA, United States (U.S.

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6225335	B1	20010501	
APPLICATION INFO.:	US 1998-212494		19981215	(!

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-659191, filed on 5 Jun

1996, now patented, Pat. No. US 5883113

Continuation-in-part of Ser. No. US 1995-485323, filed

9)

on 7 Jun 1995, now patented, Pat. No. US 5880141

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Raymond, Richard L. LEGAL REPRESENTATIVE: Foley & Lardner

NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 4036

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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IT 15966-93-5P, SU 5408 186610-93-5P, SU 5404
186610-94-6P, SU 5406 186611-14-3P, SU 5402
186611-15-4P, SU 5403 186611-16-5P, SU 5405
186611-17-6P, SU 5407 186611-29-0P, SU 5453
186611-30-3P, SU 5454 186611-31-4P, SU 5455
186611-32-5P, SU 5456 186611-33-6P, SU 5459
186611-34-7P, SU 5460 186611-37-0P, SU 5463
186611-39-2P, SU 5465 186611-48-3P, SU 5477
186611-49-4P, SU 5478 186611-50-7P, SU 5479
186611-54-1P, SU 5613 186611-56-3P, SU 5614
186611-66-5P, SU 5625 186611-67-6P, SU 5626
```

(prepn. of indolinones capable of modulating tyrosine kinase signal transduction)

RN 15966-93-5 USPATFULL

204005-46-9P, SU 5416

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline CH & N & \\ \hline Me & CH_2-CH_2-CO_2H \\ \end{array}$$

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-32-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-49-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 USPATFULL

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-54-1 USPATFULL

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-56-3 USPATFULL

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-66-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-67-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5nitro- (9CI) (CA INDEX NAME)

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 58 OF 70 USPATFULL

ACCESSION NUMBER:

TITLE:

2000:153739 USPATFULL

and methods for the treatment of disease Tang, Peng Cho, Moraga, CA, United States

INVENTOR(S): Sun, Li, Foster City, CA, United States

> McMahon, Gerald, San Francisco, CA, United States Hirth, Klaus Peter, San Francisco, CA, United States!

> Shawver, Laura Kay, San Francisco, CA, United States

Indolinone combinatorial libraries and related products

PATENT ASSIGNEE(S):

Sugen, Inc., South San Francisco, CA, United States

(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6147106		20001114	
APPLICATION INFO.:	US 1997-915366 .		19970820	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Stockton, Laura L	٠.		
NUMBER OF CLAIMS:	15			

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 42 Drawing Figure(s); 24 Drawing Page(s)

LINE COUNT:

5935

Page 371

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating, regulating and/or inhibiting protein kinase signal transduction. Such compounds are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis and restenosis and metabolic diseases such as diabetes. The present invention features indolinone compounds that potently inhibit protein kinases and related products and methods. Inhibitors specific to the FLK protein kinase can be obtained by adding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone, in particular at the 1' position of the indole ring. Indolinone compounds that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano-b-pyrrol moiety. Indolinone compounds that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosoluble indolinone compounds that are tyrosine kinase inhibitors and related products and methods.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 203988-42-5P, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-
      5,7-dibromo-2-indolinone 203988-54-9P, 3-[(3,4-Dibromo-2-
      methylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone 203988-64-1P
        3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2-
      indolinone 203988-74-3P, 3-[(3,4-Dibromo-2-methylpyrrol-5-
      yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
      203988-84-5P, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-
      [[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
      203988-94-7P, 3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-
      (morpholinosulfonyl)-2-indolinone 203989-04-2P,
      3-[(3,4-Dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-
      indolinone 203989-05-3P, 3-[[2,4-Dimethyl-3-
      (ethoxycarbonyl) \, pyrrol-5-yl] \, methylideny \bar{l} \, ]-5,7-dibromo-2-indolinone
      203989-08-6P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-
      4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5,7-dibromo-2-
      indolinone 203989-14-4P, 3-[[2,4-Dimethyl-3-
      (ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-iodo-2-indolinone
      203989-17-7P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-
      4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-iodo-2-indolinone
     203989-24-6P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-
      yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203989-27-9P,
      3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-
      [(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-bromo-4-methyl-2-
      indolinone 203989-35-9P, 3-[[2,4-Dimethyl-3-
      (ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-
      indolinone 203989-40-6P, 3-[[2-(Ethoxycarbonyl)-3-[2-
      (ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-
      yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
     203989-52-0P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-
     yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
      indolinone 203989-56-4P, 3-[[2-(Ethoxycarbonyl)-3-[2-
      (ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-
     yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
      indolinone 203989-65-5P, 3-[[2,4-Dimethyl-3-
      (ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-(morpholinosulfonyl)-2-
     indolinone 203989-68-8P, 3-[[2-(Ethoxycarbonyl)-3-[2-
      (ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-
     yl]methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203989-75-7P
       3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-(2-
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chloroethyl)-2-indolinone 203989-78-0P, 3-[[2-(Ethoxycarbonyl)-

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3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203989-88-2P,
3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-
indolinone 203989-98-4P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-
yl)methylidenyl]-5-iodo-2-indolinone 203990-08-3P,
3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2-
indolinone 203990-18-5P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-
yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203990-28-7P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203990-38-9P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203990-48-1P,
3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-
indolinone 203991-62-2P, 3-[(2,4-Dimethylpyrrol-5-
yl)methylidenyl]-5,7-dibromo-2-indolinone 203991-72-4P,
3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone
203991-82-6P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-bromo-4-
methyl-2-indolinone 203991-92-8P, 3-[(2,4-Dimethylpyrrol-5-
yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203992-02-3P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-12-5P
, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203992-22-7P, 3-[(2,4-Dimethylpyrrol-5-
y1) methylideny1] -5-(2-chloroethyl) -2-indolinone 203994-35-8P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5,7-dibromo-2-indolinone 203994-53-0P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203994-72-3P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203994-91-6P,
3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203995-11-3P, 3-[[2-Chloro-4-(methoxycarbonyl)-3-
[(methoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203995-26-0P
, 3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203995-36-2P
, 3-[[2-Chloro-4-(methoxycarbonyl)-3-[(methoxycarbonyl)methyl]pyrrol-5-
yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203995-39-5P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5,7-dibromo-2-indolinone 203995-48-6P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-iodo-2-indolinone 203995-57-7P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-bromo-4-methyl-2-indolinone 203995-66-8P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203995-75-9P, 3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-
methylpyrrol-5-yl]methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulf
onyl]-2-indolinone 203995-84-0P, 3-[[2-(Ethoxycarbonyl)-4-
(methoxycarbonyl)-3-methylpyrrol-5-yl]methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203995-93-1P,
3-[[2-(Ethoxycarbonyl)-4-(methoxycarbonyl)-3-methylpyrrol-5-
yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone 203996-03-6P,
3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone
203996-13-8P, 3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-iodo-2-
indolinone 203996-23-0P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203996-33-2P,
3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203996-43-4P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 203996-53-6P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203996-63-8P
```

RN 203988-54-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203988-64-1 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ & H & \\ Br & & \\ Me & & Br & Br \end{array}$$

RN 203988-74-3 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203988-84-5 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203988-94-7 USPATFULL

CN Morpholine, 4-[[3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203989-04-2 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 203989-05-3 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-08-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-14-4 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-17-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-24-6 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & Me \\ Br & Me & C-OEt \\ & & O & \\ & & O & \\ \end{array}$$

RN 203989-27-9 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-35-9 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-40-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-52-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-56-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-65-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-68-8 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

- RN 203989-75-7 USPATFULL
- CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

- RN 203989-78-0 USPATFULL
- CN 1H-Pyrrole-3-propanoic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

- RN. 203989-88-2 USPATFULL
- CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203989-98-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203990-08-3 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203990-18-5 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203990-28-7 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203990-38-9 USPATFULL

CN Morpholine, 4-[[3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203990-48-1 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 H
 CH
 H
 N
 Me
 Et

RN 203991-62-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203991-72-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203991-82-6 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203991-92-8 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203992-02-3 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203992-12-5 USPATFULL

CN Morpholine, 4-[[3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & H & O & H \\ \hline O & S & CH & Me \\ \hline O & Me & Me \\ \end{array}$$

RN 203992-22-7 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203994-35-8 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203994-53-0 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & &$$

RN 203994-72-3 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-chloro-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203994-91-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-11-3 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$F_3C$$
 $NH-S$
 O
 $NH-S$
 O
 $MeO-C$
 $CH_2-C-OMe$

RN 203995-26-0 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-36-2 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 203995-39-5 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-48-6 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-57-7 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-66-8 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-75-9 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-84-0 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 203995-93-1 USPATFULL

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & O \\ \hline & H & C \\ \hline & CH & N \\ \hline & CH & C \\ \hline & MeO-C & Me \\ \hline & O \\ \end{array}$$

RN 203996-03-6 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 203996-13-8 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203996-23-0 USPATFULL

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ \hline & N & O \\ \hline & CH & N \\ \hline & Et \\ \end{array}$$

RN 203996-33-2 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203996-43-4 USPATFULL

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203996-53-6 USPATFULL

CN Morpholine, 4-[[3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203996-63-8 USPATFULL

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204003-90-7 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-91-8 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-96-3 USPATFULL

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-97-4 USPATFULL

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline HO_2C-CH_2-CH_2 & CH & Me \end{array}$$

RN 204004-29-5 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_2N$$
 H_2N
 H_3N
 H_3N
 H_4N
 H_5N
 H_5N
 H_5N
 H_5N
 H_6N
 H_7N
 H_7N

RN 204004-86-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-amino-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline H_2N & O & H \\ \hline Me & CH_2-CH_2-C-OMe \\ \end{array}$$

RN 204004-92-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & \\ & & N & O & \\ & & & N & \\ & & & CH_2-CH_2-C-OMe \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & &$$

RN 204004-94-4 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 204005-03-8 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 204005-21-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,2,4-trimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 204005-38-9 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline H_2N & CH & Me \end{array}$$

RN 204005-39-0 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$H_2N$$
 H_2N
 H_3
 H_4
 H_4
 H_5
 H_6
 H_6
 H_6
 H_6
 H_7
 H_8
 H_8

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-54-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 204005-56-1 USPATFULL

CN 2H-Indol-2-one, 5-amino-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2N}$$
 H_{2N}
 H

RN 204005-58-3 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-59-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

L65 ANSWER 59 OF 70 USPATFULL

ACCESSION NUMBER:

2000:138391 USPATFULL

TITLE:

3-(substituted)-2-indolinones compounds and use thereof

as inhibitors of protein kinase

activity

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

	NUMBER	KIND	DATE	
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NUMBER DATE

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US 1997-60194P 19970926 (60)

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: ASSISTANT EXAMINER: McKane, Joseph K. Oswecki, Jane C. Lyon & Lyon LLP

LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM:

27 1

LINE COUNT:

4998

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel 3-(substituted)-2-indolinones compounds and physiologically acceptable salts and prodrugs thereof which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related disorders such as

cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4 215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ Br & & \\ Me & & Et \end{array}$$

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ N & O & \\ \hline & CH & \\ & Me & CH_2-CH_2-C-OEt \\ \end{array}$$

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{MeO} & \text{H} & \text{O} \\ \text{MeO} & \text{CH} & \text{N} \\ \\ \text{Me} & \text{CH}_2\text{-}\text{CH}_2\text{-}\text{C}\text{-}\text{OMe} \\ \end{array}$$

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 60 OF 70 USPATFULL

ACCESSION NUMBER:

2000:134906 USPATFULL

TITLE:

4-Alkenyl- and 4-alkynyloxindoles

INVENTOR(S):

Chen, Yi, Nutley, NJ, United States
Corbett, Wendy Lea, Randolph, NJ, United States

Dermatakis, Apostolos, North Brunswick, NJ, United

States

Liu, Jin-Jun, Warren, NJ, United States

Luk, Kin-Chun, North Caldwell, NJ, United States Mahaney, Paige E., Montclair, NJ, United States Mischke, Steven Gregory, Florham Park, NJ, United

States

PATENT ASSIGNEE(S):

Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S.

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION: APPLICATION INFO.:	US 6130239 US 1999-464502		20001010 19991215	(9)

NUMBER DATE

PRIORITY INFORMATION:

US 1998-112591P 19981217 (60) US 1999-149073P 19990816 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT: PRIMARY EXAMINER: Granted

LEGAL REPRESENTATIVE:

Aulakh, Charanjit S.

NUMBER OF CLAIMS

Johnston, George W., Rocha-Tramaloni, Patricia S.

NUMBER OF CLAIMS:

42

EXEMPLARY CLAIM:

1

LINE COUNT:

4523

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel 4-alkenyl- and 4-alkynyl oxindoles having the

formula ##STR1## and the pharmaceutically acceptable salts thereof, wherein R.sup.1, R.sup.2, R.sup.3, a, b, and X are as defined herein. These compounds inhibit cyclin-dependent kinases (CDKs), in particular CDK2. These compounds and their pharmaceutically acceptable salts, and prodrugs of said compounds, are anti-proliferative agents useful in the treatment or control of cell proliferative disorders, in particular cancer, more particularly, the treatment or control of breast and colon tumors. Also disclosed are pharmaceutical compositions containing the compounds of formula I and II as well as intermediates useful in the preparation of the compounds of formula I and II.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 275387-68-3P, (Z)-3-[(4-Acetyl-1H-pyrrol-2-yl)methylene]-1,3dihydro-5-fluoro-4-iodo-2H-indol-2-one 275387-99-0P
275388-01-7P 275388-18-6P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275387-68-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-iodo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-99-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-01-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-18-6 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 275387-73-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 275387-74-1 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-(methylamino)-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275387-77-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, (3Z)- (9CI) (CA INDEX NAME)

RN 275387-78-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(3-hydroxy-3-pyrrolidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

HCl

RN 275388-00-6 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(2S)-2-pyrrolidinylethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HCl

RN 275388-02-8 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[[(2S,4R)-4-hydroxy-2-pyrrolidinyl]ethynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

● HCl

RN 275388-03-9 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,3-dihydro-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & AC \\ \hline & & & \\ E \text{ ETNH} & C & & H \\ \hline \end{array}$$

HC1

RN 275388-04-0 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[(4-hydroxy-4-piperidinyl)ethynyl]-, monohydrochloride, (3Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 275388-10-8 USPATFULL

CN

1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[4-[3-(ethylamino)-1-propynyl]-5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & Me \\ \hline & V & \\ \hline & V & \\ \hline & & \\ EtNH & C \end{array} = C \\ \begin{array}{c|c} C & O & \\ \hline & & \\ \hline$$

● HCl

RN 275388-19-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-[5-fluoro-1,2-dihydro-2-oxo-4-[(2S)-2-pyrrolidinylethynyl]-3H-indol-3-ylidene]methyl]-4-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

HCl

RN 275388-31-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-5-fluoro-1,3-dihydro-4-[3-[(2-hydroxypropyl)amino]-1-propynyl]-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{OH} & & \\ & & \\ \text{Me} & & \\ \end{array}$$

HC1

RN 275388-32-4 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R,4S,5R)-4-(ethylamino)-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 275388-33-5 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(2R)-3-(ethylamino)-2-methyl-2H-pyran-6-yl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-34-6 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3R, 4S, 5R)-4-k]

amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 275388-35-7 USPATFULL

CN 2H-Indol-2-one, 3-[(4-acetyl-1H-pyrrol-2-yl)methylene]-4-[(3S,4S,5R)-4-amino-3,5-dihydroxy-1-hexynyl]-5-fluoro-1,3-dihydro-, (3Z)- (9CI) (CFINDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

IT 275388-09-5P

(prepn. of 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindole anti-proliferatives and analogs by reaction of alkynes with the corresponding 4-halo-2-oxoindoles)

RN 275388-09-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(5-fluoro-1,2-dihydro-4-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & Me \\ \hline & N & O \\ \hline & Z & N \\ \hline & H & \\ \end{array}$$
 OEt

L65 ANSWER 61 OF 70 USPATFULL

ACCESSION NUMBER:

2000:134905 USPATFULL

TITLE:

3-(cyclohexanoheteroarylidenyl)-2-indolinone

protein tyrosine kinase inhibitors

INVENTOR(S): Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S): Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

The state of the s	NUMBER	KIND DATE	
PATENT INFORMATION: APPLICATION INFO.:	US 1998-99842	20001010 19980619	(9)
	NUMBER	DATE	,)
PRIORITY INFORMATION:	US 1997-50977P US 1997-59544P	19970620 (60) 19970919 (60)	
DOCUMENT TYPE: FILE SEGMENT: PRIMARY EXAMINER: ASSISTANT EXAMINER: LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT:	Utility Granted Richter, Johann Dolan, John F. Lyon & Lyon LLP 20 1 5643		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-(cyclohexanoheteroarylidenyl)-2indolinone compounds and physiologically acceptable salts and prodrugs
thereof which are expected to modulate the activity of protein
tyrosine kinases and therefore to be useful in the prevention
and treatment of protein tyrosine kinase related
cellular disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & & CH_2-C-OMe \\ \hline & & & & \\ & & & & \\ \end{array}$$

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ Br & & \\ & & \\ Me & & \\ & & \\ Me & & \\ \end{array}$$

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\stackrel{N}{\stackrel{}}}$$
 $\stackrel{O}{\stackrel{H}{\stackrel{}}}$ $\stackrel{O}{\stackrel{}}$ $\stackrel{H}{\stackrel{}}$ $\stackrel{O}{\stackrel{}}$ $\stackrel{O}{\stackrel{}}$

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

215543-97-8 USPATFULL RN

1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & Me \\ & & & \\ Br & & & \\ Br & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

L65 ANSWER 62 OF 70 USPATFULL

ACCESSION NUMBER:

2000:47250 USPATFULL

TITLE:

3-(cycloalkanoheteroarylidenyl)-2- indolinone

protein tyrosine kinase inhibitors

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

	NUMBER	KIND DATE	
PATENT INFORMATION: APPLICATION INFO.:	US 6051593 US 1998-99721	20000418 19980619	(9)
	NUMBER	DATE	

PRIORITY INFORMATION:

19970919 (60) US 1997-59544P US 1997-50413P 19970620 (60)

Utility

DOCUMENT TYPE: FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Richter, Johann Oswecki, Jane C.

ASSISTANT EXAMINER: LEGAL REPRESENTATIVE:

Lyon & Lyon LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

20

LINE COUNT:

1 3421

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel 3-(cycloalkanoheteroarylidenyl)-2indolinone compounds and physiologically acceptable salts and prodrugs thereof which are expected to modulate the activity of protein tyrosine kinases and therefore to be useful in the prevention and treatment of protein tyrosine kinase related

cellular disorders such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5 186611-30-3 186611-31-4

186611-33-6 186611-34-7 186611-37-0

215536-87-1 215536-88-2 215536-91-7

215537-01-2 215537-24-9 215537-79-4

215543-92-3 215543-93-4 215543-94-5

215543-95-6 215543-96-7 215543-97-8

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN '186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-87-1 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215536-88-2 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215536-91-7 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 215537-01-2 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-24-9 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215537-79-4 USPATFULL

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 215543-92-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 Me

RN 215543-93-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-acetyl-3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 215543-94-5 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & N & O & \\ \hline & CH & N & \\ \hline & Me & CH_2-CH_2-C-OEt \\ \end{array}$$

RN 215543-95-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5,6-dimethoxy-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

MeO
$$\stackrel{H}{\stackrel{N}{\stackrel{N}{\longrightarrow}}}$$
 $\stackrel{O}{\stackrel{H}{\stackrel{N}{\stackrel{N}{\longrightarrow}}}}$ $\stackrel{O}{\stackrel{\parallel}{\stackrel{}}}$ $\stackrel{O}{\stackrel{\parallel}{\stackrel{}}}$ $\stackrel{CH}{\stackrel{2}{\longrightarrow}}$ $\stackrel{CH}{\stackrel{2}\longrightarrow}$ $\stackrel{C$

RN 215543-96-7 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[[4-(methoxycarbonyl)benzoyl]amino]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-

dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 215543-97-8 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

L65 ANSWER 63 OF 70 USPATFULL

ACCESSION NUMBER:

PATENT ASSIGNEE(S):

1999:99576 USPATFULL

TITLE:

Crystals of the tyrosine kinase domain of non-insulin

receptor tyrosine kinases

INVENTOR(S):

Mohammadi, Moosa, New York, NY, United States

Schlessinger, Joseph, New York, NY, United States

Hubbard, Stevan R., Riverdale, NY, United States

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

NUMBER KIND DATE PATENT INFORMATION: US 5942428 19990824 US 1996-701191 APPLICATION INFO.: 19960821 (8) DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Teng, Sally P. LEGAL REPRESENTATIVE: Lyon & Lyon LLP

NUMBER OF CLAIMS: 4 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 12 Drawing Page(s)

LINE COUNT: 31042

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Crystals of the tyrosine kinase domain of cytoplasmic tyrosine kinases and receptor tyrosine kinases that undergo ligand-mediated receptor dimerization are provided. In particular, crystals of a mutant of the tyrosine kinase domain of fibroblast growth factor receptor 1 (FLGK), alone and in complex with a non-hydrolyzable adenosine triphosphate analogue, are provided. Also provided are the high resolution three dimensional structures of crystalline FLGK, both alone and in co-complex with the adenosine triphosphate analogue, as determined by X-ray diffraction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186611-14-3D, complex with fibroblast growth factor receptor 1

(crystal structures of a protein tyrosine kinase)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
 $^{\rm O}$ $^{\rm H}$ $^{\rm N}$ $^{\rm N}$ $^{\rm Me}$ $^{\rm CH}_2-{\rm CH}_2-{\rm CO}_2{\rm H}$

L65 ANSWER 64 OF 70 USPATFULL

ACCESSION NUMBER: 1999:37134 USPATFULL

TITLE: 3-(4'-dimethylaminobenzylidenyl)-2-indolinone and

analogues thereof for the treatment of disease

INVENTOR(S): Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S): Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-485323, filed

on 7 Jun 1995

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Raymond, Richard L. LEGAL REPRESENTATIVE: Lyon & Lyon LLP

NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
LINE COUNT: 4065

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 15966-93-5P 186610-93-5P 186610-94-6P

186610-95-7P 186611-14-3P 186611-15-4P
186611-16-5P 186611-17-6P 186611-29-0P
186611-30-3P 186611-31-4P 186611-37-0P
186611-39-2P 186611-48-3P
(prepn. of 3-benzylidene-2-indolinones as tyrosine kinase activity modulators)
15966-93-5 USPATFULL
1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN

CN

RN 186610-93-5 USPATFULL
CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI)
(CA INDEX NAME)

RN 186610-94-6 USPATFULL CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186610-95-7 USPATFULL CN 2H-Indol-2-one, 3-[(4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

H N O H N Me

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3dihydro- (9CI) (CA INDEX NAME)

L65 ANSWER 65 OF 70 USPATFULL

ACCESSION NUMBER:

1999:34018 USPATFULL

TITLE:

3-(2'-alkoxybenzylidenyl)-2-indolinone and analogues

thereof for the treatment of disease

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

NUMBER DATE KIND ______ US 5883116 PATENT INFORMATION: 19990316 APPLICATION INFO.: US 1996-655224 19960605 (8)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1995-485323, filed

on 7 Jun 1995

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Raymond, Richard L. Lyon & Lyon LLP

NUMBER OF CLAIMS: 26 EXEMPLARY CLAIM: 3816

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

15966-93-5P, SU 5408 186610-93-5P, SU 5404

186610-94-6P, SU 5406 **186611-14-3P**, SU 5402

186611-15-4P, SU 5403 186611-16-5P, SU 5405

186611-17-6P, SU 5407 186611-29-0P, SU 5453

186611-30-3P, SU 5454 186611-31-4P, SU 5455

186611-37-0P, SU 5463 186611-39-2P, SU 5465

186611-48-3P, SU 5477 204005-46-9P

(3-(2-alkoxybenzylidene)-2-indolinones and their analogs for modulating tyrosine kinase signal transduction)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN . 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline & H & | \\ \hline & CH & N & C-OEt \\ \hline & O & O \\ \hline & | & | \\ \hline & EtO-C-CH_2-CH_2 & CH_2-C-OEt \\ \hline \end{array}$$

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 66 OF 70 USPATFULL

ACCESSION NUMBER:

1999:34015 USPATFULL

TITLE:

3-(4'-Bromobenzylindenyl)-2-indolinone and analogues

thereof for the treatment of disease

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

		NUMBER	KIND	DATE
PATENT INFORMATION:	US	5883113		19990316
APPLICATION INFO.:	US	1996-659191		19960605

RELATED APPLN. INFO.:

US 1996-659191 19960605 (8) Continuation-in-part of Ser. No. US 1995-485323, filed

on 7 Jun 1995

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER:

Raymond, Richard L.

LEGAL REPRESENTATIVE:

Lyon & Lyon LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 27 1

LINE COUNT:

3833

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules apable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal ell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5P, SU 5408 186610-93-5P, SU 5404

186610-94-6P, SU 5406 186611-14-3P, SU 5402

186611-15-4P, SU 5403 186611-16-5P, SU 5405

186611-17-6P, SU 5407 186611-29-0P, SU 5453

186611-30-3P, SU 5454 186611-31-4P, SU 5455

186611-37-0P, SU 5463 186611-48-3P, SU 5477

204005-46-9P, SU 5416

(prepn. of 3-benzylidene-2-indolinones as tyrosine kinase activity modulators)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & Me \\ \hline & CH & Me \\ \end{array}$$

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

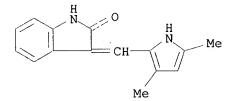
CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)



L65 ANSWER 67 OF 70 USPATFULL

ACCESSION NUMBER: 1999:30822 USPATFULL

Benzylidene-Z-indoline compounds for the treatment of TITLE:

INVENTOR(S): Tang, Peng Cho, Moraga, CA, United States

Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S): Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

NUMBER KIND DATE _____ ___ PATENT INFORMATION: US 5880141 19990309 US 1995-485323 19950607 (8) APPLICATION INFO.:

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

Raymond, Richard L. PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Lyon & Lyon LLP

NUMBER OF CLAIMS: 7 EXEMPLARY CLAIM: LINE COUNT: 2475

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to organic molecules capable of modulating AB tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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15966-93-5P, SU 5408 186610-93-5P, SU 5404
   186610-94-6P, SU 5406 186611-14-3P, SU 5402
   186611-15-4P, SU 5403 186611-16-5P, SU 5405
   186611-17-6P, SU 5407 186611-29-0P, SU 5453
   186611-30-3P, SU 5454 186611-31-4P, SU 5455
   186611-32-5P, SU 5456 186611-33-6P, SU 5459
   186611-34-7P, SU 5460 186611-37-0P, SU 5463
   186611-39-2P, SU 5465 186611-48-3P, SU 5477
   186611-49-4P, SU 5478 186611-50-7P, SU 5479
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186611-54-1P, SU 5613 186611-56-3P, SU 5614 186611-66-5P, SU 5625 186611-67-6P, SU 5626

204005-46-9P, SU 5416

(prepn. of indolinones capable of modulating tyrosine kinase signal transduction)

RN 15966-93-5 USPATFULL

1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-CN ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\text{H}}_{\text{N}}$$
 $^{\text{O}}_{\text{CH}}$ $^{\text{H}}_{\text{N}}$ $^{\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H}}$

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-32-5 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 USPATFULL

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & CH_2 - C - OMe \\ \hline & O & CH_2 - C - OMe \\ \hline \\ & O & CH_2 - C - OMe \\ \hline \\ \hline & O & CH_2 - C - OMe \\ \hline \\ \hline \\ & O &$$

RN 186611-34-7 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-49-4 USPATFULL

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 USPATFULL

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & N & Me & C-Me \\ \hline & CH_2 & \end{array}$$

RN 186611-54-1 USPATFULL

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-56-3 USPATFULL

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-66-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-67-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 68 OF 70 USPATFULL

ACCESSION NUMBER:

1998:157314 USPATFULL

TITLE:

Substituted indolylmethylene-oxindole analogues as

tyrosine kinase inhibitors

INVENTOR(S):

Battistini, Carlo, Novate Milanese, Italy Ballinari, Dario, S. Donato Milanese, Italy

Ermoli, Antonella, Buccinasco, Italy

Penco, Sergio, Milan, Italy

Vioglio, Sergio, Cusano Milanino, Italy

PATENT ASSIGNEE(S):

Pharmacia & Upjohn S.p.A., Milan, Italy (non-U.S.

corporation)

	NUMBER	KIND DATE	
PATENT INFORMATION:	US 5849710	19981215	
	WO 9632380	19961017	
APPLICATION INFO .:	US 1996-750208	19961204	(8)
	WO 1996-EP1165	19960314	•
		19961204	PCT 371 date
		19961204	PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION:

GB 1995-7298 19950407

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Richter, Johann

ASSISTANT EXAMINER: LEGAL REPRESENTATIVE: Oswecki, Jane C.

NUMBER OF CLAIMS:

Oblon, Spivak, McClelland, Maier & Neustadt, P.C. 12

EXEMPLARY CLAIM:

1

LINE COUNT:

1106 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

The present invention relates to indol-3-ylmethylene-2-oxindole derivatives which are useful as tyrosine kinase inhibitors. The compounds are suitable for use as anti-proliferative agents, anti-metastatic agents, anti-cancer agents, and in the control of angiogenesis and in inhibiting the development of atheromatous and an immunomogulating agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 184020-79-9P

(prepn. of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

RN 184020-79-9 USPATFULL

CN

Methanimidamide, N'-[2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1Hindol-5-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

L65 ANSWER 69 OF 70 USPATFULL

ACCESSION NUMBER:

1998:138936 USPATFULL

TITLE:

3-(2'-halobenzylidenyl)-2-indolinone compounds for the

treatment of disease

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States

McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

NUMBER KIND DATE PATENT INFORMATION: US 5834504 19981110

APPLICATION INFO.: RELATED APPLN. INFO.: US 1996-655225 19960605 Continuation-in-part of Ser. No. US 1995-485323, filed

on 7 Jun 1995

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Raymond, Richard L.

LEGAL REPRESENTATIVE: Lyon & Lyon LLP NUMBER OF CLAIMS: 24

EXEMPLARY CLAIM:

LINE COUNT:

3662

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

RN 186610-93-5 USPATFULL CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-03-8 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline \\ CH & N & \\ \hline \\ Me & CH_2-CH_2-C-OMe \\ \end{array}$$

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L65 ANSWER 70 OF 70 USPATFULL

ACCESSION NUMBER:

1998:95556 USPATFULL

TITLE:

3-heteroaryl-2-indolinone compounds for the treatment

of disease

INVENTOR(S):

Tang, Peng Cho, Moraga, CA, United States Sun, Li, Foster City, CA, United States McMahon, Gerald, Kenwood, CA, United States

PATENT ASSIGNEE(S):

Sugen, Inc., Redwood City, CA, United States (U.S.

corporation)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1995-485323, filed

(8)

on 7 Jun 1995

DOCUMENT TYPE: FILE SEGMENT:

LINE COUNT:

Utility Granted

PRIMARY EXAMINER: LEGAL REPRESENTATIVE: Raymond, Richard L. Lyon & Lyon LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

28 1

1 3788

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to organic molecules capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 15966-93-5P 186610-93-5P 186610-94-6P

186611-14-3P 186611-15-4P 186611-16-5P

186611-17-6P 186611-29-0P 186611-30-3P

186611-31-4P 186611-37-0P 186611-39-2P

186611-48-3P 186611-56-3P 186611-67-6P

204005-46-9P

(prepn. of 3-(hetero)arylmethylene-2-indolinones as tyrosine kinase signal transduction modulators)

RN 15966-93-5 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-93-5 USPATFULL

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{
m N}$$
 $^{\rm O}_{
m CH}$ $^{\rm H}_{
m N}$ $^{\rm N}_{
m Me}$ $^{\rm CH}_2-{\rm CH}_2-{\rm CO}_2{\rm H}$

RN 186611-15-4 USPATFULL

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 USPATFULL

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 USPATFULL

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 USPATFULL

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 USPATFULL

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 USPATFULL

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline & N & O \\ \hline & CH & N & C-OEt \\ \hline & O & O \\ \hline & & & \\ EtO-C-CH_2-CH_2 & CH_2-C-OEt \\ \end{array}$$

RN 186611-48-3 USPATFULL

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-56-3 USPATFULL

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-67-6 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 H
 O_1
 O_2
 O_3
 O_4
 O_4

RN 204005-46-9 USPATFULL

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

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